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SYMPOSIUM: CHEMOTHERAPY AND ANTIBIOTICS*

CHEMOTHERAPY AND ANTIBIOTICS

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It is obviously not possible to cover all of the important aspects of chemotherapy and antibiotics in this presentation. It will be necessary to limit this discussion to some general principles which may help the physician to understand the problems involved and to orient him with respect to the practical uses of these agents. Certain aspects of special interest will also be considered, particularly with respect to those agents which have had wide clinical use. Many important features of the subject will necessarily have to be omitted or mentioned only very briefly.

SULFONAMIDE CHEMOTHERAPY

The first successful use of drugs of this group was based on the demonstration of antistreptococcal activity in the azo dye, prontosil. It was soon shown that the active principle of prontosil was the simple compound, para-aminobenzine sulfonamide which is released from prontosil in the body. This compound, now known as sulfanilamide, has had wide and successful use in the treatment of many infections, particularly those caused by the streptococcus, gonococcus, and meningococcus and also in urinary tract infection due to the colon bacillus. It is also effective against a large variety of other organisms but usually to a lesser extent. In pneumococcal infections, it often proved lifesaving in the treatment of cases of meningitis due to this organism and also in some cases of pneumonia due to type 3 strains, but it was not highly effective in most pneumococcal pneumonias.

Among the favorable features of sulfanilamide are its great penetrating power and its high solubility. Since it is excreted by the kidneys, either unchanged or in the acetylated form, concentrations up to about one per cent are possible and frequently attained in the urine without local complications except under unusual circumstances. Sulfanilamide, however, has many drawbacks. When compared with its more recent derivatives its activity is much more limited and it produces toxic effects of greater severity and more frequently. Those particularly characteristic of sulfanilamide are the cyanosis which is constant, hemolytic anemia which occurs more frequently with this than with other related compounds, nervous symptoms which may be quite disturbing, and occasionally severe liver damage.

Changes in the structure of sulfanilamide made by the addition on the para-amino group tend to inactivate the drug unless the added groupings split off in the body to release the active compound. Acetylation occurs by conjugation in this position within the body and the acetylated sulfonamides are inactive. The addition of various groupings on the sulfonamide end, however, produces profound changes in the sol-

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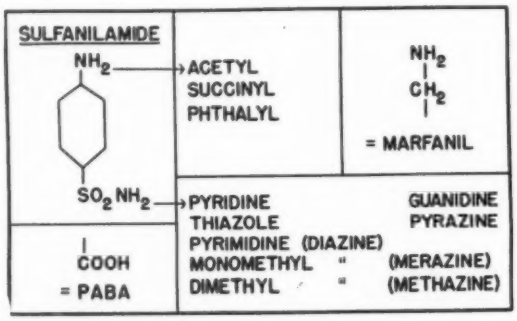
ubility, absorption and excretion, toxicity and activity. Compounds of the latter type have proved to be the most successful among the many that have been synthesized and tested. See Fig. 1 below.



Sulfapyridine was the first such compound to receive clinical trial. It has greater activity than sulfanilamide against the pneumococcus and also against some other organisms including the staphylococcus. Though it lacked the cyanosis-producing property of sulfanilamide, sulfapyridine produced such marked nausea and vomiting and its low solubility resulted in such frequent occurrence of crystalluria, hematuria and renal colic that it rapidly lost favor in this country, particularly after the appearance of sulfathiazole and later sulfadiazine. Sulfapyridine was used continuously by the British throughout most of the war, perhaps because they had a large supply on hand or because they were the ones who first introduced it.

Sulfathiazole proved to be appreciably more active against the pneumococcus, staphylococcus and coliform organisms and also produced much less nausea and vomiting. Drug fever and rashes, which are probably manifestations of sensitization reactions, were much more frequent with this compound. Sulfathiazole, too, is highly insoluble and, in addition, it is excreted more rapidly than sulfapyridine. As a result, precipitation of the drug occurs all too frequently with resulting complications similar to those that were observed with sulfapyridine. When given intravenously in the form of the sodium salt, particularly in a dehydrated patient, precipitation sometimes occurs directly in the renal tubules giving rise to complete anuria without crystalluria or hematuria. Another result of the rapid excretion is the lower blood levels which result from comparable doses when compared with sulfapyridine and sulfadiazine. In addition, sulfathiazole shows much poorer penetration than sulfanilamide, sulfapyridine and sulfadiazine as indicated by the relatively low concentrations of the drug in the cerebrospinal fluid. It has, therefore, not been recommended for use in meningitis, although its greater antibacterial properties and relatively low toxicity make it fully as effective as sulfanilamide and sulfapyridine.

Sulfadiazine, the pyrimidine derivative of sulfanilamide, has proved to be the best compound now available from the point of view of its high antibacterial properties and relatively low toxicity. It is rapidly absorbed, penetrates about as well as sulfapyridine into the crebrospinal fluid and is excreted more slowly than the previous compounds mentioned. The blood concentrations from the same dose are, therefore, relatively higher. In addition, only a relatively small proportion is bound to serum protein and the acetylated compound is rapidly excreted so that the proportion of inactive drug in the circulating blood is low, except in patients who have poor renal function. Sulfadiazine, has, therefore, come to be used more widely than all the other compounds. It has most of the toxic effects common to the others, although it gives no cyanosis, produces hemolytic anemia extremely rarely and nausea and vomiting quite infrequently. Its relatively low solubility, however, does result in urinary tract complications. In common with the other sulfonamides, it produces sensitization reactions that is, fever and rashes, when given continuously for more than five days and occasionally agranulocytosis if given for more than two weeks.

Three compounds closely related to sulfadiazine are of interest as indicating the effect of minor differences in chemical structure. Sulfamerazine, the only one of these three that has been used to any great

extent, is sulfadiazine to which one methyl group has been added in the pyrimidine ring. This compound is still absorbed quite rapidly but its excretion is much more delayed and as a result higher blood levels are maintained. This was considered to be desirable because of the possibility of using less frequent doses and smaller total amounts. Doses of one gram every eight hours were advocated instead of the usual one gram every four hours. The smaller amount, however, proved much less effective in spite of quantitatively similar or even higher blood levels as compared with sulfadiazine. The percentage of the acetylated form of sulfamerazine in the serum is much higher than with sulfadiazine and furthermore, a larger proportion of the free drug is apparently bound to the serum albumin which further limits its activity. As a result, larger doses were necessary than were at first thought adequate and the resulting higher blood levels and slower excretion increased the frequency of toxic effects.

Another compound first introduced by the British and widely used by them toward the end of the war is sulfamethazine which is similar to sulfamerazine except that it has two methyl groups instead of one. This compound is absorbed and excreted much more rapidly but is acetylated to a greater extent than either of its diazine analogues. Consequently, blood levels are much lower with the same dose, and hence larger doses are required for therapy. This in turn results in much more frequent crystalluria and hematuria in spite of the greater solubility of both its free and acetylated forms as compared with the corresponding forms of sulfadiazine and sulfamerazine.

The pyrazine group has a molecular structure identical with pyrimidine except for the position of the nitrogens. Sulfapyrazine is a highly active compound but it is much less soluble than sulfadiazine, more rapidly absorbed and more rapidly excreted and only slightly acetylated. The resulting blood levels are even lower than those obtained with sulfathiazole, and urinary tract complications due to precipitation are, therefore, more frequent. For this reason this compound has not received wide acclaim, although even with the low levels this drug seems to be as active as any other compound.

Two features of special interest with respect to the use of sulfonamides may be mentioned because they are not widely or fully appreciated. One is concerned with the problem of sensitization and the other with the renal complications.

The development of fever or a rash and occasionally other symptoms during sulfonamide administration usually indicates the development of sensitization and in the majority of individuals this sensitization will persist. Continuation of the therapy aggravates the symptoms and readministration of the same compound at a subsequent date will bring about a recurrence of symptoms and these are often of great severity and may preclude the use of that drug. It has been found, however, that other sulfonamide compounds may then be used either to continue treatment without interruption or for subsequent therapy at a later date in the great majority of cases. Only about 15 percent of persons who develop these reactions to one of the agents will become so sensitized that they will not tolerate any other sulfonamide compound in addition to the one which occasioned the sensitization in the first place.

Thus, a person who develops a rash and fever from sulfadiazine can receive sulfathiazole immediately to continue treatment and the fever and rash will subside or he can be given sulfathiazole at a later date without having any manifestations provided, of course, that he has not previously had sulfathiazole long enough to become sensitized to it as well. In the case of the three compounds, sulfadiazine, sulfamerazine and sulfamethazine, however, there is a reciprocal relationship so that sensitization to one almost always is accompanied by sensitization to all three. Sulfapyrazine, on the other hand, may be given to a person sensitized to sulfadiazine or to one of its methyl derivatives without recurrence of

symptoms, and the reverse is also true. Persons sensitive to sulfapyrazine will tolerate any of the diazine compounds.

The most frequent complications of the sulfanilamide derivatives thus far discussed are related to their low solubility which results in the precipitation of crystals of the free and acetylated forms within the urinary tract, giving rise, in turn, to hematuria and concretions which then produce renal colic and anuria. It has been found that in water or in urine, each of these compounds retains its own solubility irrespective of the presence or of the amount of any of the other sulfonamides in the same solution. Furthermore, the antibacterial action of any combination of sulfonamide drugs was found to be additive. These facts have led to the suggestion that combinations of sulfonamides may be used to advantage in therapy. The same total dose in the form of a combination of different sulfonamides would have the same activity but would be much less likely to produce urinary tract complications than if a single compound were used.

Lehr in New York suggested the use of a combination of sulfadiazine and sulfathiazole and Frisk in Sweden suggested a combination of equal amounts of sulfadiazine, sulfamerazine and sulfathiazole. Because sulfamerazine is excreted more slowly and sulfathiazole more rapidly than sulfadiazine the Frisk combination results in absorption and excretion relationships almost identical to those obtained with sulfadiazine. Flippin and his colleagues used sulfadiazine and sulfamerazine, a combination which has the merit of two compounds which are mutually related as far as sensitization is concerned, leaving the possibility of using sulfathiazole later should a reaction result from the use of that combination. This would not be possible if the combinations suggested by Lehr and Frisk were used because in that event the patient would most likely be sensitized to both the diazine and thiazole derivatives. Possibly the combination of the three pyrimidine compounds, sulfadiazine, sulfamerazine and sulfamethazine might prove even better since this combination, like Frisk's, is likely to have absorption and excretion relationships similar to those obtained with sulfadiazine.

For use in enteric infections or for reducing the bacterial content of the bowel, it has seemed desirable to have compounds which are poorly absorbed and yet remain active in the bowel or become active by the release of an active component within the bowel contents. Several different compounds have been used. The first was sulfaguanidine which is highly soluble but poorly absorbed from the bowel. This compound has been widely used but it is much less effective as a bacteriostatic than other compounds and is sufficiently absorbed to give most of the common reactions, including those in the urinary tract. The latter are particularly prone to occur in patients with diarrhea or in tropical climates because the drug is often administered to patients who become dehydrated and excrete very little urine.

Other compounds have been made by additions on the para-amino group of sulfathiazole to form succinylsulfathiazole (sulfasuxidine) and phthalylsulfathiazole (sulfathalidine). These compounds are inactive until they are hydrolyzed in the bowel and the free sufathiazole is released. Only a very small part of the total amount of the drug ingested is broken down in this manner but this occurs mostly low in the bowel where the sulfathiazole is poorly absorbed and therefore is almost entirely available for action on the bowel contents. Since, however, some material may be broken down higher up in the bowel and since some absorption does take place from lower down, the possibility of sensitization to sulfathiazole exists and actually does occur at times.

A similar result is obtained by a compound in which a COOH group is added to the thiazole ring. This group too is released within the bowel so that activity is probably due to the free sulfathiazole. Carboxysulfathiazole, however, is very poorly absorbed and, when taken by mouth, is recoverable almost entirely in the feces. Other changes in the thiazole ring as in the

case of sulfathiadiazole and one of its methyl derivatives result in much more rapid and much more complete absorption and excretion in the urine in humans. These latter compounds though active in reducing the bowel flora in mice proved less useful in this respect in humans but may possibly be effective in the treatment of urinary tract infections. Because of the rapidity with which these compounds are excreted in the urine, however, the use of large doses at any one time must be avoided if crystalluria and renal colic is to be prevented.

It is difficult to leave the subject of sulfonamides without noting the nature of the chemical groups which are involved in the various active derivatives. The most widely accepted theory of the action of chemotherapeutic agents is that they interfere in any of a number of ways with metabolites essential to the growth of bacteria. In the case of sulfonamides it is considered to be an interference with the normal metabolism of para-aminobenzoic acid which has such a marked similarity to the structure of sulfanilamide. The other structures that have served to enhance the activity of sulfanilamide will be recognized as essential parts of the molecules of known vitamins and coenzymes.

The group of compounds not inhibited by para-aminobenzoic acid need only be mentioned. The amino grouping in these compounds is separated from the benzene ring. Such compounds were first synthesized in Germany during the war and used topically in the treatment of wound infections. They have proved too toxic for systemic use. The type compound is marfanil. These compounds, while they have been studied in this country, have not received wide acceptance because of their toxicity.

The prophylactic use of sulfonamides has received some attention. In this connection it is necessary to distinguish several distinct situations:

1. The use of a single dose or a single short course for protection against a single exposure as in the prophylaxis of gonorrhea or in the preparation for an operation on the bowel where spillage of bowel contents may be expected.

2. A single dose or a single short course for a large group of persons exposed to a possible epidemic due to a highly susceptible organism as in the case of the mass and simultaneous prophylaxis in a military camp or other large population unit for the purpose of eradicating meningococcal carriers.

3. Continuous treatment with small daily doses for individuals or for small groups of individuals for a specific indication, as in the prevention of hemolytic streptococcal infections in susceptible persons who are subject to recurrences of rheumatic fever.

4. Mass prophylaxis of a large population with the idea of preventing or reducing the general incidence of bacterial infections as in the case of military units during and immediately after mobilization, when epidemics of respiratory infections, including streptococcal infections may be expected to occur with considerable regularity.

The experiences with sulfonamide prophylaxis to date probably justify the following conclusions:

A single dose of one to four drams or a short course for one or two days is probably not harmful except in two circumstances, namely: (1) in persons who have already been sensitized to the same or sometimes to another sulfonamide by virtue of a previous exposure, and (2) in persons with severe renal damage who will retain the drug for long periods even after these small amounts. Such a dose will probably clear up meningococcal carriers temporarily and prevent infection from exposure to, or during the incubation period of meningococcal infections. It may possibly prevent other infections due to highly susceptible strains of gonococcus, meningococcus, or hemolytic streptococcus and will probably reduce the incidence and severity of postoperative peritonitis following bowel surgery.

Continuous prophylaxis may result in sensitization of an appreciable proportion of individuals and agranulocytosis or other serious complications in a small percentage.

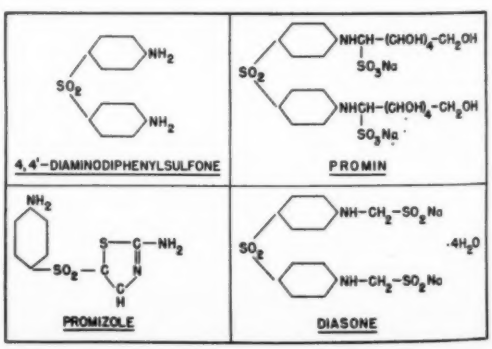
These complications may be serious in themselves and usually will preclude the further use of these compounds. This method may also permit the dissemination of sulfonamide-resistant strains while suppressing or eliminating susceptible ones. Whether the resistant strains that spread are those which were originally resistant or strains which were enhanced in their resistance by exposure to the drug within the body is not entirely clear from the evidence to date. Probably either or both of these possibilities may be operative in this instance. Continuous treatment will probably completely eliminate the chance of the recipient's acquiring meningococcal infections and will reduce the incidence of bacterial respiratory tract infections in these individuals unless or until sulfonamide-resistant strains make their appearance. Recurrent attacks of rheumatic fever should, therefore, be prevented to some extent by such prophylaxis.

The importance of drug fastness is well demonstrated by the striking increase in the proportion of resistant strains of gonococci during the last few years. At the present time very few susceptible gonococci are encountered whereas resistant strains were quite rare before 1939. The increased incidence of resistant strains of hemolytic streptococci during and after the prophylactic sulfonamide program in some of the armed forces has also been quite striking. Resistant strains of pneumococci have been found to disseminate during continuous sulfonamide prophylaxis against respiratory infections and such resistant pneumococci and hemolytic streptococci may cause serious infections which will resist therapy with any of the sulfonamides.

The evidence to date would indicate that natural resistance to sulfonamides or fastness acquired by exposure of bacteria to sulfonamides within the body is a permanent property of the organism and is not lost on passage. The virulence of strains that are resistant under these conditions is not reduced. This is in contrast to the course of certain organisms which are made resistant to sulfonamides by exposure to these drugs *in vitro*; such organisms may lose their virulence in the process of acquiring resistance and they may regain their susceptibility when freed from exposure to the drug for a number of generations.

It is worth pointing out that resistance to one of the sulfonamides is accompanied by similar resistance to others when allowance is made for the different degrees of the underlying bacteriostatic action of the different compounds against the particular organism concerned. This is in contrast to what has already been noted in the case of sensitization. Sulfonamide resistance, however, whether natural or acquired does not alter the susceptibility of the organisms to other types of chemical agents and to the various antibiotics.

Brief mention may be made here of the use of chemotherapy in tuberculosis. The sulfonamides are capable of suppressing the growth of *Mycobacterium tuberculosis* in synthetic media and they have a slightly favorable influence on the lesions produced by virulent human strains in a standard type of infection in the susceptible guinea pig. The latter effect, however, has not been very significant. Several compounds, however, have proved effective in such experimental infections. One of them is 4-4′ diaminodiphenylsulfone and two others are derivatives of this compound, namely promin and diasone. A fourth compound, promizole, has also proved highly effective in guinea pigs. The latter compound is very similar in structure to sulfathiazole from which it differs only by the position of one NH_2 group. The formulas of these compounds are shown in Fig. 2 below. In human



cases the use of all of these compounds has been sharply limited chiefly because of their considerable toxicity. The use of effective doses for long enough periods to bring about favorable results comparable to those observed in guinea pigs has not yet been possible in large numbers of cases. The results, however, are encouraging enough to continue the search along similar lines. The possibility of using these compounds, or similar ones in conjunction with streptomycin or other substances that may become available also requires further and careful study since there is evidence to suggest that such a combination may be helpful and feasible.

Having mentioned the sulfones it seems appropriate also to note the use of para-aminobenzoic acid in the treatment of rickettsial infections. This substance is effective in experimental infections, particularly in chick embryos, but also to some extent in mice. It is excreted very rapidly in the latter and in humans and for that reason frequent and large doses are required to maintain any appreciable concentration in the blood and tissues. With the use of the sodium salt in large and frequent doses, favorable results have been reported in cases of epidemic typhus and possibly in Rocky Mountain spotted fever and in scrub typhus.

PENICILLIN

The virtues and properties of penicillin as an antibiotic agent are now well known. Its effectiveness against most gram-positive organisms is appreciably superior to that of the sulfonamides. It is far more effective than the latter in gonococcal infections and is equally effective against sulfonamide-resistant strains as against those which are sulfonamide sensitive. For that reason penicillin has essentially replaced the sulfonamides in the treatment of gonococcal infections. The closely related meningococci, however, are considerably less sensitive to penicillin and much more sensitive to the sulfonamides, and sulfonamide-resistant strains of meningococci have not been encountered. The sulfonamides, therefore, continue to be the drugs of choice in the treatment of meningococcal meningitis and other meningococcal infections.

Penicillin is not effective against most of the gram-negative bacilli. Occasional strains may be sufficiently susceptible so that local therapy using high concentrations may be successful. Thus occasional cases of *H. influenzae* meningitis and of gram-negative bacillus empyema have been cured by the use of penicillin given respectively by the intrathecal and intrapleural routes in addition to the systemic administration.

Penicillin is highly effective against many spirochetal infections. When used locally or systemically it produces dramatic results in cases of fusospirochetal infection of the mouth. Systemic treatment is highly effective in yaws and in relapsing fever. The results in Weil's disease are variable. When used in large enough doses given over a long enough period, it has produced a high percentage of cures in syphilis. The optimum dose and duration of therapy have not been entirely worked out. Combined therapy with arsenic and bismuth has proved superior to the use of penicillin alone and probably constitutes the most reliable form of therapy at present. While recent work indicates that experimental syphilitic infections in the rabbit may be prevented by relatively small doses of penicillin G, there is at present no evidence to support the hope that similar results may be expected in humans. Syphilis has developed in patients who have been successfully treated with small doses of penicillin for gonococcal infections. In such cases the appearance of the primary luetic lesion may be delayed or prevented, but serological and clinical evidence of the disease appears later.

All of these features of the antiluetic action are independent of the changing character of penicillin which caused much concern not so long ago. The lots of penicillin now available are essentially devoid of the relatively inactive penicillin K and consist almost entirely of penicillin G which seems to be the most effective form available at present. Whether other forms of penicillin or other antibiotics from the same

or other molds will have greater antisyphilitic action remains to be seen.

Penicillin does not appear in significant concentrations in the cerebrospinal fluid after parenteral injection and for that reason intrathecal injections must be used to supplement parenteral injections in the treatment of meningitis. Furthermore the sulfonamide drugs because of their great penetration and their different mode of action are highly useful as an adjunct to penicillin in such cases.

The sulfonamides are inhibited by pus and by the products of tissue break-down. For that reason the local instillation of sulfonamides into suppurative foci has not usually proved of any great advantage. Penicillin, on the other hand, can be used very effectively by local application or instillation into areas of suppuration. It has proved particularly effective when used in this manner in the treatment of serous sac infections, namely in empyema, purulent arthritis and pericarditis. In such cases repeated aspirations followed by instillations of penicillin in generous amounts have resulted in a large proportion of cures without resort to operations. At the Boston City Hospital almost all cases of post-pneumonia empyema due to penicillin-susceptible strains have been successfully treated in this manner during the past two years and the usual mutilating operations have not been found necessary. As much as 200,000 units is injected daily into the empyema cavity in a volume of 10 to 100 c.c. of saline. Lavage of the cavity before each instillation has proved advantageous particularly when the fluid is thick and contains much fibrin. When large doses are given intrapleurally, additional penicillin by intramuscular injection is usually unnecessary becase the absorption from the cavity is slow, and significant blood levels of penicillin are often sustained for 24 hours, or even longer. Aspirations and intrapleural injections are continued as long as improvement continues and until a few days after the infection has definitely been controlled as evidenced by all clinical and laboratory criteria.

In osteomyelitis, particularly in the acute forms but also in chronic cases after the lesion has been freed of sequestra by operative procedures, the prolonged use of large doses of penicillin has brought about consistently good results. The best results follow prolonged and intensive treatment and avoidance of operation as long as clinical and laboratory findings indicate that the infection is controlled and in spite of apparent progression of the lesion in x-rays. The eventual return of the bony structure to normal usually occurs in such cases. Penicillin resistant strains sometimes appear but the degree of resistance is not marked and improvement often continues in spite of the presence of such organisms. In the early postoperative stages in chronic cases, instillations of penicillin t h r o u g h small catheters inserted into the w o u n d have proved helpful.

In subacute bacterial endocarditis due to susceptible organisms the keynote is the same, namely prolonged and intensive treatment. A minimum of four weeks of treatment after the temperature has returned to normal should be insisted on in such cases. The tendency now is to use massive doses but the majority of cases will not require more than a total of 500,000 units a day given in six or eight doses. Only occasional cases due to relatively resistant strains may require larger amounts. The development of resistant strains during treatment has not been frequent and the degree of enhanced resistance has been minor. Occasionally cases which apparently fail to respond to small doses may respond to doses of several million units per day. Others will respond to penicillin X or to streptomycin when they failed to respond to penicillin G but these cases are rare.

The problem of dosage now is considerably different from what it was when penicillin was scarce and very expensive. The general tendency has been to use much larger amounts than are indicated from the sensitivities of the infecting organism and also from the known results in large numbers of cases. There is, of course, no serious objection to such usage, except that it is usually unnecessary, extravagant and

wasteful. One aspect that has interested us is the use of large individual doses in aqueous solutions and the possibility of thereby increasing the interval between injections and reducing the number of injections. The penicillin that is now available gives very little local reactions and can be used in high concentrations so that large amounts may be injected in small volumes without much local irritation. It has been possible to effect cures in most cases of pneumococcal pneumonia with 100,000 units every eight hours. Though effective levels are not usually maintained in the blood for more than half of the interval between injections the results seem to justify this procedure. Similar adjustments for increasing the dose and prolonging the interval may be adapted to other infections or to severe cases.

Large doses of penicillin given at frequent intervals, however, may broaden the scope of penicillin activity to include infections with organisms usually considered to be penicillin resistant. This possibility is suggested by the apparently successful use of such dosage in cases of peritonitis. Doses of 100,000 or 200,000 units every two or three hours will limit the spread of such infection and often effect cure even though the gram-negative bacilli and enterococci usually found in these cases are not very susceptible to penicillin *in vitro*.

Various methods are available for prolonging penicillin action by delaying its excretion and some of these methods have received wide use. The one now most popular is the preparation of penicillin in a mixture of 4.8 per cent beeswax in peanut oil. While it has been widely claimed that a single dose of 300,000 units in such a mixture will maintain effective blood levels in adults throughout a 24 hour period, this has not proved true in the majority of cases. Indeed, blood levels after 12 hours are very erratic, and only a small proportion of patients still have measurable amounts circulating after 18 hours. The preparations have another disadvantage in that they are often difficult to give, especially if vials containing more than a single dose are used; the local reactions are sometimes moderate or severe and persist for a long time, and sensitization reactions are more frequent from their use than after simple aqueous preparations. New preparations in which the same ingredients are prepared so that they flow freely at room temperature are probably not quite so effective from the point of view of sustaining levels though they are much more convenient to administer. In some sick patients as much as 600,000 units twice a day may be necessary to obtain results similar to those ordinarily observed with 30,000 units of aqueous preparations given every three hours. Preparations containing less than 4.8 per cent beeswax, or none at all as in the products depending on water-in-oil emulsions, have produced too little prolongation of levels to warrant the effort and expense. Far better results are obtained by a substantial increase in the dose of penicillin.

Other agents have been used which prolong the action of penicillin by interfering with its tubular excretion. Diodrast was the first one to be used experimentally. Para-aminohippuric acid also has this effect, but it must be used intravenously in large amounts. Sodium benzoate and restriction of fluid intake have been found useful for this purpose by some workers. Recently a new compound called caronamide has been found to have a similar effect but large and frequent oral doses of this compound are necessary. The details of its practical use remain to be worked out particularly with respect to the possibility of enhancing the action of penicillin taken orally.

Penicillin given orally in simple aqueous solutions produces measurable blood levels fairly constantly if given on an empty stomach, but four or five times as much is required on the average to produce results comparable to those obtained after intramuscular administration. The gastric acidity and motility, inactivation by intestinal bacteria and possibly adsorption on food are all variable factors which may interfere with the proper absorption of oral penicillin. The absorption after meals is extremely erratic and usually unpredictable. Some

persons will obtain no measurable levels even from large doses and the amount recovered in the urine may vary from 2 to 35 per cent of the administered dose. Buffered penicillin tablets are preferable when given after meals and seem to give more consistent results. There seems to be no significant or consistent difference among the various types of buffers. Sodium citrate has been used most frequently but it may occasionally give nausea especially in children. Capsules or coated tablets are undesirable because the site of their disintegration varies in different individuals and the absorption will be minimal if that disintegration takes place below the duodenum.

Simple and uncomplicated infections with susceptible organisms such as acute gonorrhea, pneumococcal pneumonia and streptococcal pharyngitis will respond to oral penicillin if the dose is large enough and given frequently but not within one and a half or two hours after a meal. Oral penicillin, however, cannot be relied upon in the severer infections, particularly those with less sensitive organisms such as the staphylococci.

Penicillin may also be given as an aerosol and this method is being widely used in the treatment of suppurative diseases of the lungs and bronchi. Aqueous solutions of as much as 100,000 units per c.c. and probably even more concentrated solutions of the crystalline penicillin that is now available can be given without local irritation. High penicillin concentrations are thus attained locally wherever the mist penetrates and perhaps up to 25 per cent of the inhaled material is absorbed into the blood and recoverable in the urine. The peak levels in the blood occur early, and demonstrable amounts are found for only short periods, usually one or two hours. The results in certain cases of putrid lung abscess and in diffuse bronchiectasis are quite striking if such treatment is given four to eight times a day for a period of four weeks or longer. In patients who produce large volumes of sputum postural drainage preceding each inhalation considerably enhances the efficacy of the treatment. It may also be used with benefit before operations on the lungs.

Penicillin in large doses has been found effective in the treatment of experimental infections with certain rickettsiae and with some strains of the lymphogranuloma venereum-psittacosis group of viruses. The virus of lymphogranuloma venereum and the immunologically related viruses of trachoma and inclusion blenorrhea, are also susceptible to sulfonamide drugs but most of the psittacosis group are not. Of local interest is the fact that the strains of the psittacosis-like virus that were responsible for the recent outbreaks of pneumonitis in Louisiana and California and which produced such a high mortality are among the ones that have shown definite though not marked susceptibility to penicillin. The results of treatment of infections with these agents in humans have not been very striking though there is no wide experience and possibly the doses used have not been adequate.

The prophylactic use of penicillin has not received attention in the past but may be widely applied in the near future. One or more injections of 50,000 or 100,000 units just before and after tooth extractions or other dental manipulations in patients with rheumatic or congenital heart disease may minimize the chances of developing bacterial endocarditis. The use of penicillin (and sulfonamides, too) during severe influenza virus infections or in cases of extensive viral pneumonia may also prove useful in preventing the occurrence or spread of the highly fatal bacterial complications. The use of penicillin in the prophylaxis of venereal infections is an obvious corollary to its use in the treatment of these diseases, but no reliable data on the effectiveness of such prophylaxis is now available. The possible complications of its widespread use and particularly the potentialities for producing or disseminating resistant strains are virtually unknown.

STREPTOMYCIN

Streptomycin was the product of a systematic study undertaken deliberately in an attempt to discover antibiotics which are

effective against the gram-negative bacilli and the mycobacteria, since most infections with these organisms proved not to be highly susceptible to penicillin and to the available chemicals. When it was first discovered and found to be active against both of these groups of organisms, it was hoped that streptomycin would provide the missing link in the conquest of the bacterial diseases. This hope has not been entirely fulfilled. Nevertheless, streptomycin has proved quite useful although when compared with penicillin, both from the point of view of activity and toxicity, it is quite disappointing.

It is well to bear in mind from the very start the relative effectiveness of penicillin and streptomycin. This is indicated in the very definition of their units, the sensitivity of various strains, the range of dosage that has been found effective and the limits of tolerance. The unit of penicillin was originally defined as that amount which completely inhibits the growth of 50 c.c. of a standard staphylococcal culture. It is now defined by weight as the equivalent of 0.6 microgram of pure crystalline penicillin G. Most strains of gonococcus and hemolytic streptococcus are sensitive *in vitro* to between 0.01 and 0.04 unit or the equivalent of 0.006 and 0.024 microgram. Most staphylococci are sensitive to concentrations between 0.02 and 0.2 unit, that is, between 0.012 and 0.12 microgram. Most cases of acute gonococcal urethritis will be cured by a total of 100,000 units, or 60 milligrams of penicillin G. A case of pneumococcal pneumonia will require a total of between 300,000 and 500,000 units or 180 to 300 milligrams of penicillin. Larger doses than these are now widely used but they are not necessary and are given only because that can be done without danger. Indeed, the maximum tolerated dose of penicillin in humans is virtually unknown.

The unit of streptomycin was originally defined as that amount which will inhibit the growth of 1 c.c. of a culture of *E. coli*. It is now defined as one microgram of pure streptomycin base. Very few gram-negative bacilli are sensitive to less than 1 unit and most of the so-called sensitive strains require between 3 and 15 units. Doses of streptomycin are usually given in grams and the average adult receives between two and six grams a day for most of the susceptible infections. These amounts probably approach the minimum effective dose and nevertheless will be more than ten times the usual dose of penicillin by weight. Furthermore, the maximum tolerated dose of streptomycin is not much more than twice this amount. The cost per million units in sterile vials is very nearly the same for the two agents.

Streptomycin is, nevertheless, a valuable addition to the group of agents which are used for the definitive treatment of infectious diseases, particularly since it is effective in a number of infections which are benefitted little if at all by other available agents. Streptomycin has proved most effective in cases of acute tularemia. It has also produced cures in a large percentage of cases of meningitis due to gram-negative bacilli particularly *H. influenzae*. It is useful in many other gram-negative bacillus infections particularly those of the urinary and respiratory tracts. Typhoid fever, Salmonella infections and brucellosis, however, have not responded favorably. In certain cases of coccal infections which have failed clinically to respond to sulfonamides and penicillin or in which organisms were resistant to these agents, streptomycin has proved useful as a second line of defense.

The present consensus in regard to the role of streptomycin in the treatment of human tuberculosis is that it exerts a palliative effect by producing some degree of bacteriostasis. Most patients who have active infection with fever show decided clinical improvement within the first two weeks after treatment is started. The immediate results generally have been most striking in the miliary, meningeal and laryngeal forms of tuberculosis. The meningeal form is not benefitted unless the drug is given intrathecally as well as intramuscularly. The disease requires large doses, probably a minimum of two to three grams a day in adults for prolonged periods. Treatment

should not be undertaken unless adequate amounts of streptomycin are available to permit continuous therapy for at least three to four months. The development of resistant strains has been very frequent and has limited the effectiveness of this agent. It is generally agreed that streptomycin cannot be regarded as a substitute for present methods of sanatorium and surgical therapy.

From the point of view of the community as a whole it is probably wise, for the present, to limit the use of streptomycin in tuberculosis to the few clinics where carefully controlled and prolonged treatment and study is possible. Only on the basis of the results in such controlled groups of cases may one expect to determine the real and permanent value of streptomycin in the various forms of tuberculosis. The results of such studies carried on over a sufficiently long period may clarify the limits of usefulness and the best method of employing streptomycin both in individual cases and in groups of cases. The possibility of the use of combinations of streptomycin with the sulfone drugs also requires extensive study before any general program is suggested.

It is important to emphasize that general hospitals, particularly with the crowded conditions now prevalent, are not equipped to handle this problem and should not be expected to do so. It is still too soon to recommend any long range program even for the specialized institutions. In the meantime, it is hoped that better, more effective, less expensive and less toxic agents will become available. In particular, it is hoped that some effective agent will be discovered with which the development of resistance will not be such a prominent feature.

In the treatment of the urinary tract infections due to gram-negative bacilli the most important limiting factors from the point of view of streptomycin therapy has been the rapid development of extreme degrees of resistance in the organisms during the course of treatment. These resistant organisms persist once they appear and, as a result, the infections either fail to improve or relapse. Increases in the dose of streptomycin fail to prevent the appearance of resistant strains in spite of the fact that levels are maintained in the blood which are higher than those required by the *in vitro* sensitivity of the strains. Of course most of the patients in whom streptomycin has been used have had chronic infections with associated structural defects which interfered with successful therapy and predisposed to recurrence of infection in those who were apparently improved.

It has been shown that streptomycin is considerably more effective *in vitro* in an alkaline than in an acid medium. In the cases which were studied at the Boston City Hospital, it was noted that in those patients in whom failure to respond to streptomycin was associated with the development of resistant strains, the urine had been acid before treatment was started and throughout the course of streptomycin therapy. An attempt, therefore, was made to determine the effect of alkalis on the urine in such cases. In most instances sodium bicarbonate and potassium citrate usually six grams of each a day in four or six divided doses were given in an attempt to maintain a pH of 7.5 in the urine throughout the period of therapy. In some cases as much as ten grams of each of these alkalis were required to obtain this result. On this regime most patients showed a good bacteriological and clinical response to streptomycin and resistant strains were encountered much less frequently.

The results in certain cases of meningitis have been particularly noteworthy. Streptomycin alone has proved more effective than the combination of specific antiserum and sulfadiazine in cases of *H. influenzae* meningitis. We have had only one death in 16 consecutive cases and the majority of these patients were under one year of age and had positive blood cultures before streptomycin treatment was started. Many of them had previously failed to respond to treatment with penicillin and sulfadiazine and some of those due to type b strains had also received specific antiserum.

Although there is some penetration of

streptomycin from the blood stream into the cerebrospinal fluid, especially in cases of meningitis, the concentrations are quite low. Cases have been reported in which meningitis has developed during the course of treatment with streptomycin. For these reasons streptomycin treatment of meningitis whether due to gram-negative bacilli or to *Mycobacterium tuberculosis* must include both intrathecal and intramuscular injections. Intrathecal doses of 50 to 100 milligrams in a volume of 5 to 10 c.c. of cerebrospinal fluid or saline have been given every 12 to 24 hours in adults. In infants injections of 25 to 50 milligrams have been given intraspinally and 25 milligrams have been injected into the ventricles through the fontanelles and seem to be well tolerated.

Cures have been obtained in the majority of cases of meningitis due to various gram-negative bacilli other than *H. influenzae* and we have observed one instance of apparent recovery in a case of tuberculous meningitis. Similar results have been obtained by others. In the cases of meningitis the effectiveness of streptomycin was readily apparent by the rapid disappearance of organisms first from the smears and then from cultures of cerebrospinal fluid. Blood cultures usually become negative after the first intramuscular dose. The sugar content of the spinal fluid rises rapidly. The cell count and the protein content of the spinal fluid drops progressively and the percentage of polynuclears drops and this is accompanied by a corresponding increase in the proportion of lymphocytes. Almost all of the patients with meningitis that have been treated with streptomycin have had a drop in their temperature and marked clinical improvement in from one to four days. Fever often recurs and then persists until the streptomycin is discontinued. Resistant strains have not been encountered in any of the cases of meningitis due to *H. influenzae* that we have studied although this has been observed in a number of cases by others. We have observed the development of resistance during treatment in a case of meningitis, due to *Pseudomonas aeruginosa*.

In the cases of respiratory tract infections streptomycin has been used by intramuscular injection or as an aerosol. The latter has been reserved mostly for the chronic suppurative types of infection and the usual dose has been from 100 to 200 milligrams in 1 or 1.5 c.c. of distilled water. These aerosol treatments are given four to eight times a day. Resistant strains have developed in a case in which the streptomycin was given only by aerosol, but they have appeared after intramuscular injections alone or after combined therapy. In one case in which streptomycin and penicillin were used in succession Friedländer bacilli and pneumococci both became resistant during streptomycin treatment but neither of these organisms became resistant to penicillin given in smaller doses over a similar period in spite of the fact that these organisms persisted throughout the entire course of treatment.

The results of streptomycin treatment in pulmonary infections have varied and here again the appearance of resistant strains appeared to be the greatest limiting factor. In cases of chronic respiratory infections the underlying pathology is not altered but the infection may be limited or halted and healing promoted so that at least the progression of the disease may be arrested.

Streptomycin is not absorbed from the bowel. When given by mouth it reduces the fecal flora markedly. Oral streptomycin has, therefore, been used successfully in preparation for large bowel surgery and in the treatment of bacillary dysentery.

The toxic effects of streptomycin have not been very frequent except in patients who received large doses over prolonged periods. The local reactions from intramuscular injection include pain, tenderness and induration at the site of the injections, often accompanied by local redness and heat. They are more severe after subcutaneous injection and may be somewhat reduced by incorporating procain in the injection. Occasionally these reactions are followed by generalized muscular pains and malaise. Intrathecal injections sometimes give an increase in pleocytosis at first and if the dose

is too large there may be an increase in pressure. Earlier and probably impure lots gave more serious complications but these are no longer encountered.

The most common contitutional reaction is a histamine-like effect consisting of headache, flushing of the skin, nausea, vomiting, fall in blood pressure and occasionally convulsions. These were more frequent with the early impure lots and are rarely encountered after intramuscular injections at present but may be observed if the streptomycin is given intravenously at too rapid a rate. These reactions may apparently be avoided by the use of benadryl and possibly with pyribenzamine. Skin eruptions and fever may appear and these may take on various forms including exfoliative dermatitis and they may recur on subsequent administration of streptomycin. Streptomycin should usually be discontinued when these reactions appear.

The most striking and most disturbing toxic effect of streptomycin has been the changes in vestibular function and this apparently is a property of streptomycin itself and not of any of its impurities. The incidence of this reaction in humans varies but recent reports indicate that up to 90 per cent of persons receiving streptomycin in the treatment of tuberculosis may be affected. Patients may complain first of dizziness, light headedness, or giddiness, particularly when they change position. The loss of vestibular response as judged by a positive Romberg test and by the response to the caloric and rotation tests has persisted in most of the patients in whom treatment was continued for some time after the symptoms began. Patients may compensate, however, for this defect by other postural mechanisms so that the symptoms will usually persist and be incapacitating for only one to three months. Other toxic effects are minimal. The other serious sequellae which have been observed in patients who have recovered after treatment for tuberculous meningitis and occasionally other forms of meningitis are probably the effects of the meningitis rather than the toxic effects of the drug in most instances.

CONCLUSION

It seems proper to emphasize one point which is not fully appreciated nowadays. Throughout this presentation references were made to specific types of bacteria, to sensitivity of different strains and to blood levels of the antibacterial agents. All of these features of antibacterial therapy must be interpreted as indicating that laboratory control is still an important and essential part of the intelligent and proper management of infectious diseases. The extent to which laboratory methods are used will vary, of course, with the particular needs and the available facilities. It would be unfortunate indeed if the wide effectiveness of these chemicals and antibiotics were interpreted as indicating that laboratory diagnosis and follow-up are no longer needed in the conduct of cases of bacterial infection. The specific aspects of the use of the agents that have been discussed should indicate quite forcefully that the reverse is true.

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THE SURGICAL USE OF CHEMOTHERAPEUTIC AND ANTIBIOTIC AGENTS

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The surgical specialists of today are probably more skeptical than any other group of the therapeutic advantages of presently available antibacterial therapy. It is only natural that this should be so. The prerogative of treating infections responding solely to antibacterial agents has been usurped by the internist and general practitioner. The surgeon is consulted only when the infection is clinically persistent in spite of adequate chemotherapy or antibiotic therapy. Under such conditions it is usually possible for the surgeon to find an abscess, a focus of necrotic tissue, or an infected thrombus requiring surgical treatment. An important consequence of this clinical trend of altered responsibility is the development of funda-

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mentally different philosophies regarding antibacterial therapy by the surgical and non-surgical specialists. The internist and general practitioner look upon antibacterial therapy as a measure of primary importance, whereas the surgeon relegates it to an adjuvant position. Unquestionably, many infections are adequately treated solely by the administration of the proper antibacterial drug. By the same token many infections could be more effectively treated by surgical means alone. Hence, as is always true in conflicting philosophies, there is some question as to the relative value of the various antibacterial agents.

Even among surgeons there has been considerable controversy as to the merits of systemic chemotherapy as compared with topical applications. Again the source of the debate is to be found in a differing point of view. On the one hand, there were those concerned primarily with sterilization of the wound and disappearance of bacteria in the smear and culture. The other group sought to obtain healing of the wound regardless of its bacterial population. Both were motivated by a fundamental instinct of human nature—a desire to do something directly to the wound. At the moment the controversy seems to have been settled by the surgical experience of World War II. It has been established that local chemotherapy is not only unnecessary but frequently undesirable. Under the protection of systemically administered antibacterial agents, debridement of both recent and infected wounds has been shown to be practical and safe. In other words, the instinctive urge to treat the wound has been directed toward early closure instead of toward bacterial sterilization of the wound.

Clinical experience has justified the creation of two separate categories of surgical infection: invasive infection and wound suppuration. The surgically important and frequent types of invasive infection are those due to the hemolytic Streptococcus, Staphylococcus, and toxigenic Clostridiums. Suppuration of wounds is usually due to a mixed or polybacterial infection. Although the organisms responsible for invasive infection may be found in wound suppuration, they are rarely acting in their capacity as invasive pathogens. Furthermore, wound suppuration is not dependent upon the presence of potentially invasive pathogens. The organisms important in wound suppuration are proteolytic. The most frequently encountered types of proteolytic bacteria are *Bacillus proteus*, *Pseudomonas* (pyocyaneus) and *Clostridium sporogenes*. These organisms either are initially resistant or rapidly acquire resistance to presently available chemotherapeutic agents. Since they lack invasive attributes, their presence in the wound is dependent upon the availability of a pabulum of devitalized tissue or exudate protein. An important observation during the recent war was recognition that a blood clot was as acceptable as devitalized muscle for the growth of anaerobic bacteria. From these observations it has been concluded that the best means of treating wound suppuration is to rid the wound surgically of devitalized tissue and blood clot. The great surgical advantage of antibacterial therapy in wound management lies in the capacity of these drugs to protect living tissue from further destruction by invasive bacteria during periods of surgical manipulation. If the objective of chemotherapy is recognized as the protection of living tissues from the hazard of invasive infection, then the systemic route is the desirable method of treatment. Within such a concept of management of open wounds there is no place for topical applications of antibacterial agents.

It is pertinent at this time to comment upon another controversial matter. Some internists still advocate the intrapleural injection of chemotherapeutic or antibiotic agents in the management of empyema. Most surgeons have abandoned this practice. It is practical to consider empyema in two phases: the pleural abscess and pleural cellulitis. Even if it is granted that an occasional abscess may be sterilized by the topical instillation of such drugs as penicillin, it must be recognized that non-drainage methods prevent optimal functional rehabilitation of the underlying lung. Bacterial

sterilization of a wound must not take precedence over functional restoration of the affected part. The second type of empyema may be classified as pleural cellulitis with effusion. It is this type of empyema which responds dramatically to repeated aspirations of fluid with injections of antibacterial drugs. It has been my clinical experience that this type of infection responds equally well to continued systemic therapy with repeated pleural aspirations without supplemental local instillations of penicillin. Most of the observations regarding delayed diffusion of antibacterial agents into the pleural or serous cavities refer to the normal and not to the inflamed serous surface. It has been repeatedly demonstrated that in the presence of inflammation there is increased diffusibility of antibacterial agents into the area of inflammation.

Especially important for surgical consideration is the pathogenicity of coliform bacteria. The ease of isolation and the preferential growth of these organisms on artificial media have, in my opinion, unduly emphasized their importance. With the exception of the relatively infrequent paracolon-aerobacter, these bacteria are lacking in invasive and proteolytic characteristics. As such, they are more properly classified as commensal, or saprophytic, bacteria. Their persistence in an infection has been correlated with the presence of the intermediary products of protein break-down. In wounds such products are usually the metabolic by-products of the biologic activity of other organisms. Only in serum, urine, bile, and spinal fluid is there a sufficient metabolic substrate of small molecular nitrogenous compounds to support the survival and growth of these bacteria. In the management of wounds it is usually possible to suppress the exudation of serum by pressure dressings. The control of these organisms presents no specific problem in wound management if exudation is arrested. Specific chemotherapy designed to arrest the survival and growth of coliform bacteria is justified only in the management of infections of the urinary tract, biliary tract, and cerebrospinal system.

The saprophytic role of coliform bacteria has been established with greatest certainty in the treatment of peritonitis. There is now abundant clinical and experimental evidence to conclude that streptomycin, either alone or as adjuvant antibiotic therapy, fails to alter the course of peritonitis dramatically. On the other hand, penicillin given in dosage as great as 100,000 units every hour, according to the severity of the case, has been sufficiently effective to establish the gram-positive bacteria as the important pathogens in peritonitis. In consequence of clinical experience with the antibacterial therapy of peritonitis, it is possible to draw one further significant conclusion. Even more important than bacterial contamination is the escape of activated digestive enzymes into the free peritoneal cavity. In the surgical treatment of peritonitis, primary attention is directed to excision of necrotic tissue and exteriorization of intestinal fistulas. Once this has been achieved, the peritoneum has an extraordinary capacity to deal with the residual factor of bacterial contamination. Undoubtedly, this is accomplished more expeditiously if penicillin is given in adequate doses, and the clinical results are extremely satisfactory. Certainly there is no need for the *routine* administration of another antibacterial agent, either a sulfonamide or streptomycin. At the present time it is our practice to give supplemental streptomycin therapy (0.5 gm. every four hours) only to those desperately ill patients in whom the likelihood of fatal issue justifies the use of all conceivably helpful adjuncts to established therapeutics.

The surgeon of today is grateful for the therapeutic advantages offered by presently available drugs. Hemolytic streptococcal and staphylococcal infections are now adequately treated with minimal debility and rapid convalescence. Anaerobic cellulitis and gas gangrene present less formidable problems than previously. The surgeon also looks to the future, and knows what he wants in the way of new antibiotic compounds. Most urgently needed is an agent

for the control of infections produced by Clostridium sporogenes, Pseudomonas and Bacillus proteus. Within present concepts of reparative wound management, the new compound should be effective when given systemically. It is significant to note that none of the currently experimental compounds, including bacitracin, meets these needs. It seems likely that penicillin will remain the antibiotic of choice in surgical treatment for a considerable time to come. Current clinical investigations suggest that immediate advances may be made by continued upward revision of present dosage programs for such resistant infections as peritonitis and bronchopulmonary suppuration. It is known that dosages of 25,000,000 to 40,000,000 units of penicillin per day may be given safely.

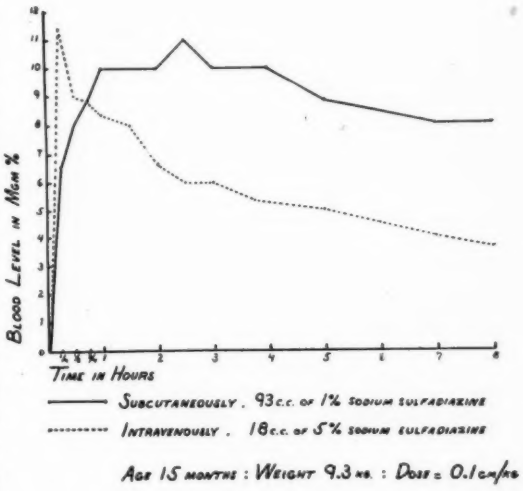
Blood Level in Mgm %
Time in Hours
Subcutaneously . 93 c.c. of 1% sodium sulfadiazine
Intravenously . 18 c.c. of 5% sodium sulfadiazine
Age 15 months : Weight 9.3 kg. : Dose = 0.1 gm/kg

Fig. 1: Comparison of blood levels to be obtained from the subcutaneous and the intravenous administration of sodium sulfadiazine. Levels as whole blood free sulfadiazine. After several injections higher levels are built up, but this serves to illustrate the type of curve obtained by each method.

USE OF ANTIBIOTICS IN PEDIATRICS

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I have greatly enjoyed the informative presentations of the preceding speakers. Since they have covered the subject so well and since the time alloted to this symposium is growing short, I shall restrict my remarks to a few case presentations. These are cases that have been seen either by my colleagues or myself in the past few years. They have been selected because they illustrate some particular problem, not because they were handled in an ideal manner or because we are particularly proud of them. Some of these cases have appeared in previous reports. The charts used to illustrate the cases contain only pertinent material —negative tests and procedures being, in general, omitted.

First, I should like to show a chart (see figure 1) which explains why we prefer the subcutaneous to the intravenous route for parenteral administration of sulfonamides. A more even, better maintained level follows subcutaneous administration. One-third of the 24 hour dose should be injected subcutaneously at eight hour intervals. We usually employ a one or two per cent solution of the sodium salt in saline or lactate-Ringer's. Oral therapy should not be relied on exclusively in severe infections.

We had one patient with pneumococcal meningitis complicating acute mastoiditis. Since this case, as well as some of the others, was seen before the supply of penicillin became plentiful, the doses used seem small when compared with those used in the past year. We have not, however, increased the dose of intrathecal penicillin and still employ 10,000 or 20,000 units dissolved in 10 c.c. of saline once or twice daily.

Figure 2 illustrates a case of pneumococcal meningitis with two relapses. Since the original attack and each of the relapses were treated differently this case actually illustrates three modes of therapy. The original attack was treated with sulfadiazine alone and the response was satisfactory. When the route of administration was changed to rectal the blood level fell to 2 mg. per cent. When the sulfadiazine was discontinued the disease relapsed within 48 hours. The first relapse was treated with sulfadiazine and systemic administration of

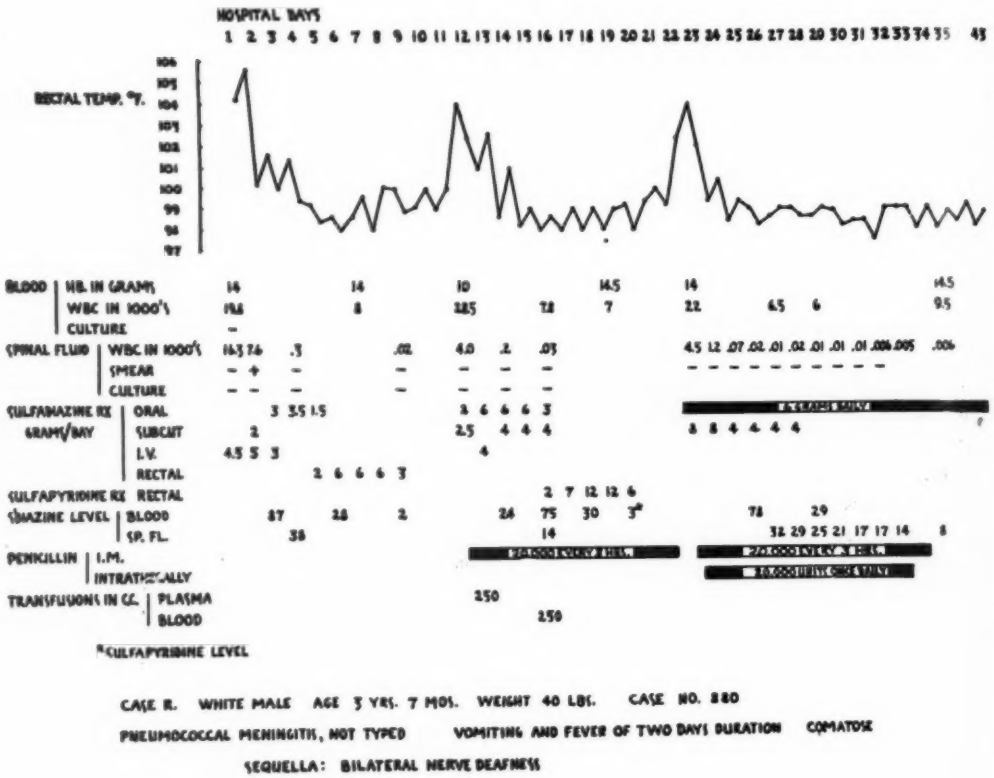


Fig. 2: See text.

penicillin. However, when the route of administration of the sulfonamide (which had been changed to sulfapyridine) was changed to rectal the blood level fell to 3 mg. per cent. When the sulfonamide was discontinued the second relapse began within 24 hours. This second relapse actually began while the child was receiving 20,000 units of penicillin intramuscularly every three hours. The treatment of the second relapse was different in two respects. This time intrathecal penicillin was administered and the oral administration of sulfadiazine was continued well into the period of convalescence. Among several lessons to be learned from this case are: (a) in treating meningitis, sulfadiazine should be continued after the patient has made a clinical recovery; (b) the rectal route of administration does not consistently provide a satisfactory blood concentration; (c) intrathecal therapy is essential—this child actually relapsed while receiving intramuscular penicillin.

Figure 3 illustrates an interesting disease, sodoku, the Spirillum minus variety of rat-bite fever (the other variety is caused by the streptobacillus moniliformis). Sodoku responds readily to penicillin as here demonstrated. Notice that after penicillin was started the lesions became worse. This is a Herxmeimer or flare-up effect; it has also been noted following the treatment of this disease with arsenicals.

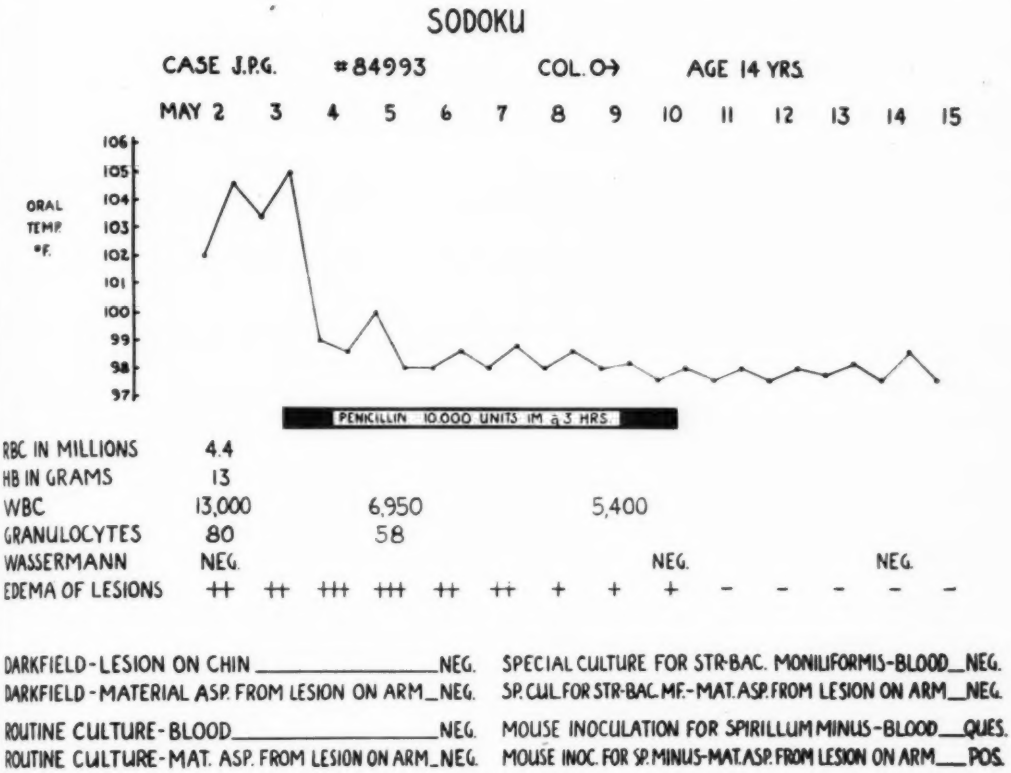

SODOKU
CASE J.P.G. #84993 COL. O→ AGE 14 YRS.
MAY 2 3 4 5 6 7 8 9 10 11 12 13 14 15
ORAL TEMP °F.
106 105 104 103 102 101 100 99 98 97
PENICILLIN 10,000 UNITS IM q 3 HRS.
RBC IN MILLIONS 4.4
HB IN GRAMS 13
WBC 13,000 6,950 5,400
GRANULOCYTES 80 58
WASSERMANN NEG. NEG. NEG.
EDEMA OF LESIONS ++ ++ +++ +++ ++ ++ + + + - - - - -
DARKFIELD-LESION ON CHIN ____ NEG.
DARKFIELD-MATERIAL ASP. FROM LESION ON ARM_NEG.
ROUTINE CULTURE-BLOOD____ NEG.
ROUTINE CULTURE-MAT. ASP. FROM LESION ON ARM_NEG.
SPECIAL CULTURE FOR STR-BAC. MONILIFORMIS-BLOOD__NEG.
SP. CUL. FOR STR-BAC. MF.-MAT. ASP. FROM LESION ON ARM__NEG.
MOUSE INOCULATION FOR SPIRILLUM MINUS-BLOOD___QUES.
MOUSE INOC. FOR SP. MINUS-MAT. ASP. FROM LESION ON ARM___POS.

Fig. 3: Sodoku treated with penicillin.

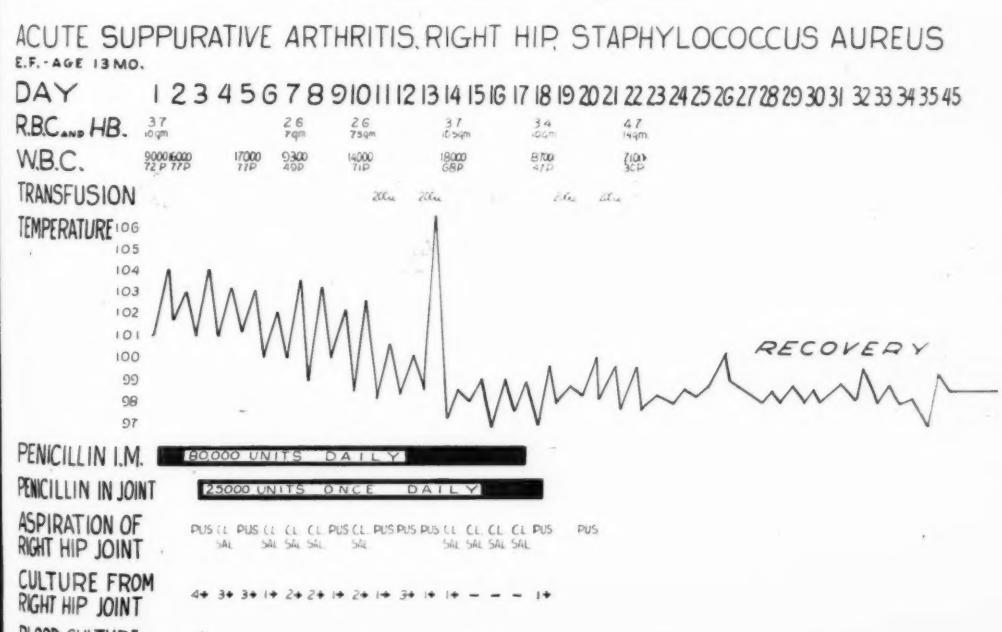
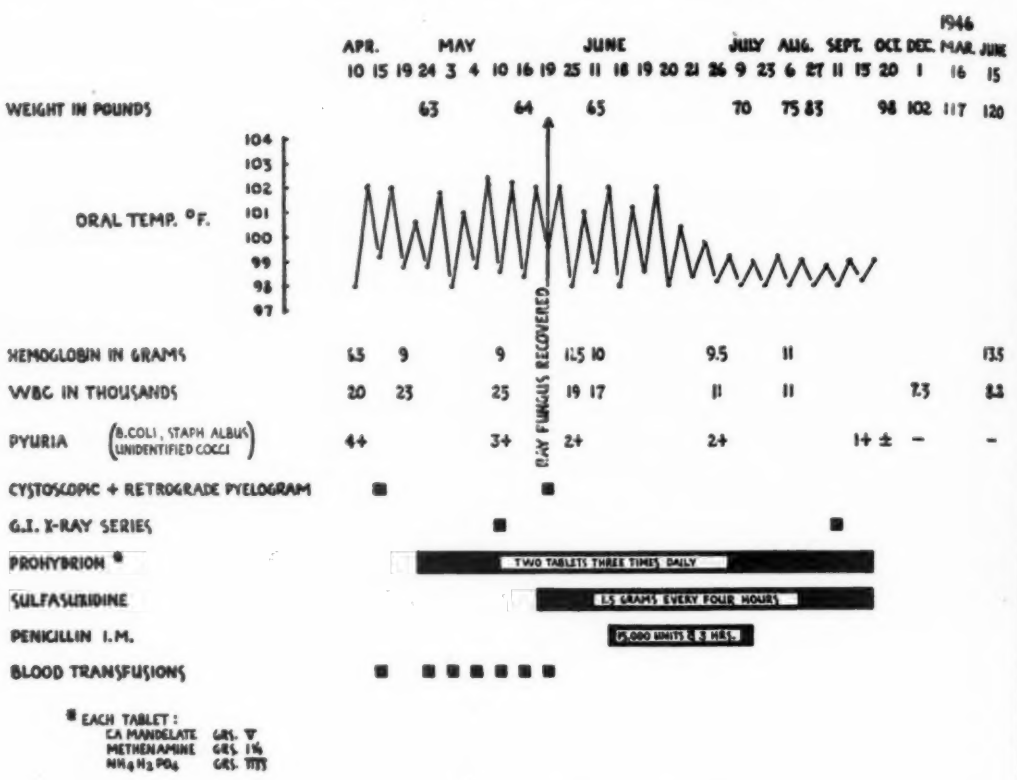

ACUTE SUPPURATIVE ARTHRITIS, RIGHT HIP, STAPHYLOCOCCUS AUREUS
E.F. - AGE 13 MO.
DAY 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 45
R.B.C. AND HB. 3.7 10 gm 2.6 7 gm 2.6 7.5 gm 3.1 8.5 gm 3.4 9 gm 4.7 14 gm
W.B.C. 9000 6000 72 P 77 P 17000 77 P 9300 49 P 14000 71 P 18000 68 P 8700 47 P 7101 35 P
TRANSFUSION 20cc 20cc 20cc 20cc
TEMPERATURE 106 105 104 103 102 101 100 99 98 97
RECOVERY
PENICILLIN I.M. 80,000 UNITS DAILY
PENICILLIN IN JOINT 25000 UNITS ONCE DAILY
ASPIRATION OF RIGHT HIP JOINT PUS CL SAL PUS CL SAL CL SAL CL SAL PUS CL SAL PUS PUS PUS CL SAL CL SAL CL SAL CL SAL PUS PUS
CULTURE FROM RIGHT HIP JOINT 4+ 3+ 3+ 1+ 2+ 2+ 1+ 2+ 1+ 3+ 1+ 1+ - - - 1+
BLOOD CULTURE - +

Fig. 4: Pyogenic arthritis treated without surgical drainage.


APR. MAY JUNE JULY AUG. SEPT. OCT. DEC. 1946 MAR. JUNE
10 15 19 24 3 4 10 16 19 25 11 18 19 20 21 26 9 23 6 27 11 15 20 1 16 15
WEIGHT IN POUNDS
63 64 65 70 75 83 98 102 117 120
ORAL TEMP. °F.
104 103 102 101 100 99 98 97
RAY FUNGUS RECOVERED
HEMOGLOBIN IN GRAMS
13 9 9 11.5 10 9.5 11 13.5
WBC IN THOUSANDS
20 23 25 19 17 11 11 7.3 8.3
PYURIA (B.COLI, STAPH ALBUS UNIDENTIFIED COCCI)
4+ 3+ 2+ 2+ 1+ ± − −
CYSTOSCOPIC + RETROGRADE PYELOGRAM
G.I. X-RAY SERIES
PROHYDRION *
TWO TABLETS THREE TIMES DAILY
SULFASUXIDINE
1.5 GRAMS EVERY FOUR HOURS
PENICILLIN I.M.
BLOOD TRANSFUSIONS
* EACH TABLET:
CA MANDELATE GRS. ½
METHENAMINE GRS. 1½
$NH_4H_2PO_4$ GRS. ⅓

CASE C.W., 15 YR. WHITE ♀, NO. 84531

Fig. 5: Abdominal actinomycosis treated with penicillin.

Figure 4 illustrates a particularly severe case of pyogenic arthritis caused by *Staphylococcus* aureus. It was treated without surgical drainage. Penicillin was given systemically and once daily locally in the hip joint, following aspiration. The rather slow response may be due to the rather small intramuscular doses that were being used when this child was treated. The temperature spike on the thirteenth day was part of a transfusion reaction.

Figure 5 illustrates a case of abdominal actinomycosis. There were fistulae from the intestinal tract to the genito-urinary tract (resulting in a severe pyuria) to the abdominal wall. The temperature record does not attempt to outline her day by day course, but rather selected typical days. Consecutive days are, however, included for a few days immediately following the institution of systemic penicillin therapy.

Fig. 6: Cavernous sinus thrombophlebitis treated with penicillin, sulfadiazine, and anti-coagulants: before treatment.

Figure 6 is the photograph of a nine year old boy with a severe case of cavernous sinus thrombophlebitis. The blood culture was repeatedly positive for staphylococcus albus. The case was treated with penicillin, sulfadiazine, and anticoagulants. Figure 7 is another photograph taken following recovery.

Fig. 7: Cavernous sinus thrombophlebitis, after treatment.

Figure 8 illustrates a case of meningitis due to type B, *Hemophilus influenzae*. It is likely that the penicillin used had little or no effect on the course of the disease. It has been included on the chart for the sake of accuracy, however, since it was used. Note that the infant was responding nicely to sulfadiazine. When streptomycin was obtained (at that time it had to be flown from New York by special request) the sulfadiazine was discontinued. While receiving streptomycin alone (both intramuscularly and intrathecally) the disease relapsed. It is well known now that many cases of influenzal meningitis do not respond to streptomycin. In this disease streptomycin should not be used to the exclusion of other forms of therapy.

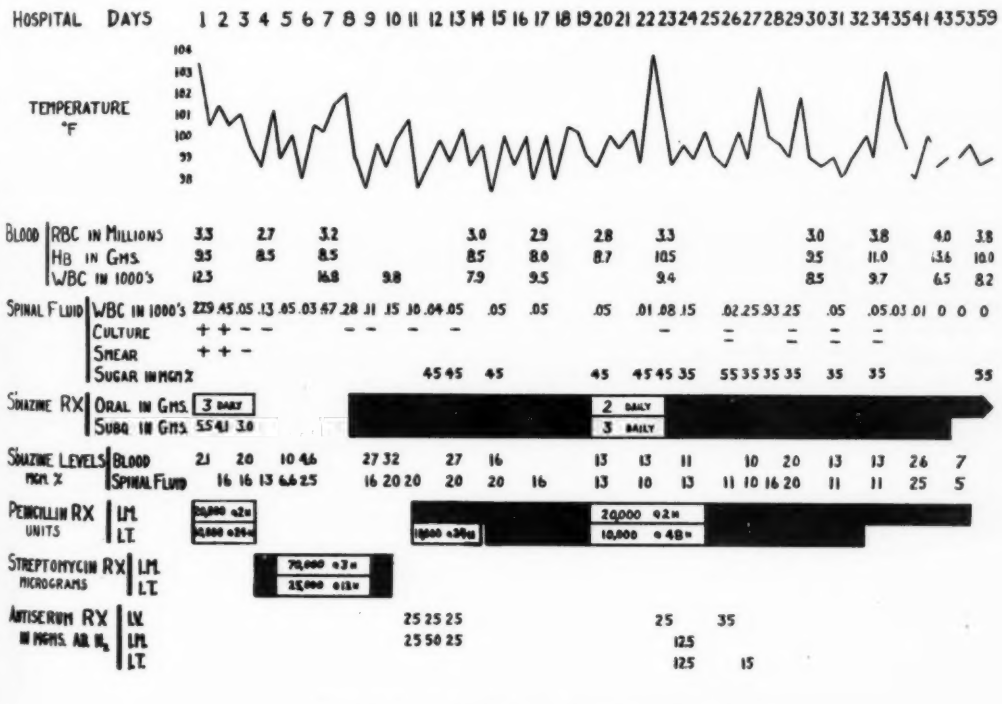


Fig. 8: See text.

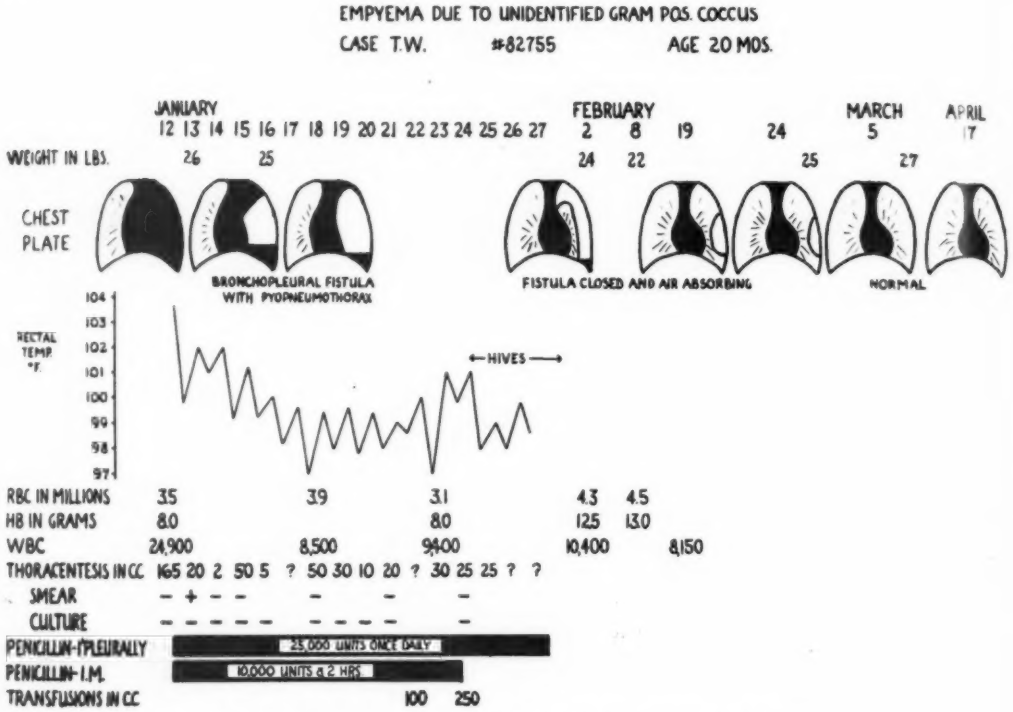

EMPYEMA DUE TO UNIDENTIFIED GRAM POS. COCCUS
CASE T.W. #82755 AGE 20 MOS.
JANUARY
12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27
FEBRUARY
2 8 19 24
MARCH
5
APRIL
17
WEIGHT IN LBS.
26 25 24 22 25 27
CHEST PLATE
BRONCHOPLEURAL FISTULA WITH PYOPNEUMOTHORAX
FISTULA CLOSED AND AIR ABSORBING
NORMAL
RECTAL TEMP °F.
104 103 102 101 100 99 98 97
←HIVES→
RBC IN MILLIONS 3.5 3.9 3.1 4.3 4.5
HB IN GRAMS 8.0 8.0 12.5 13.0
WBC 24,900 8,500 9,400 10,400 8,150
THORACENTESIS IN CC 165 20 2 50 5 ? 50 30 10 20 ? 30 25 25 ? ?
SMEAR – + – – – – –
CULTURE – – – – – – – – – –
PENICILLIN-I PLEURALLY 25,000 UNITS ONCE DAILY
PENICILLIN-I.M. 10,000 UNITS q 2 HRS
TRANSFUSIONS IN CC 100 250

Fig. 9: Empyema thoracis treated without surgical drainage.

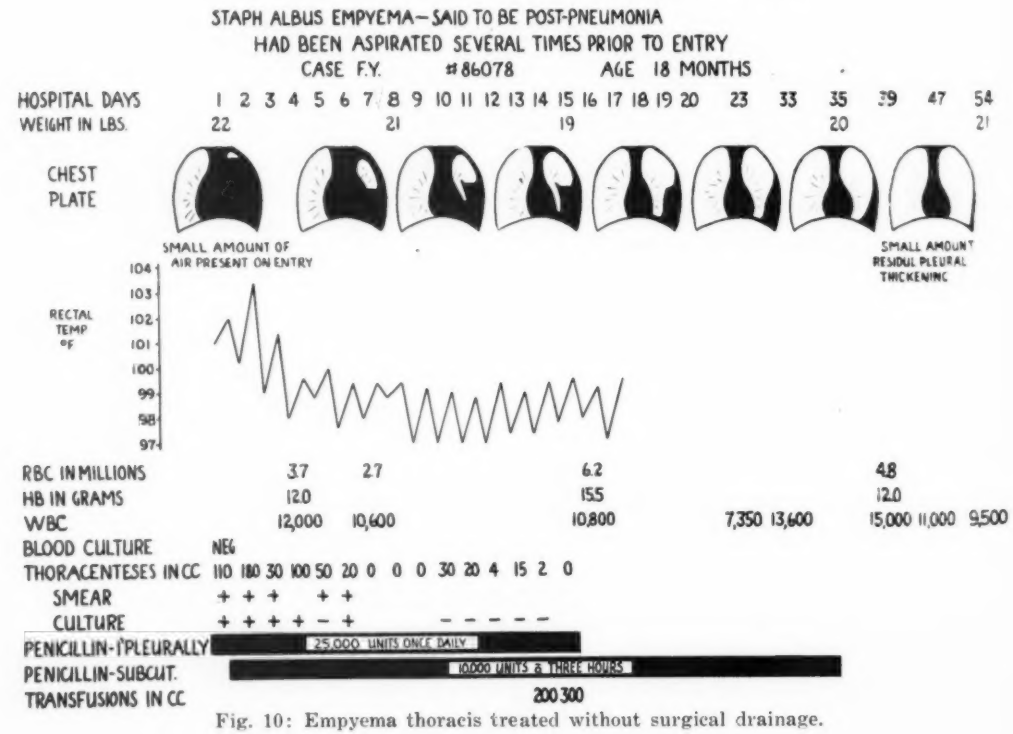

STAPH ALBUS EMPYEMA—SAID TO BE POST-PNEUMONIA
HAD BEEN ASPIRATED SEVERAL TIMES PRIOR TO ENTRY
CASE F.Y. #86078 AGE 18 MONTHS
HOSPITAL DAYS
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 23 33 35 39 47 54
WEIGHT IN LBS.
22 21 19 20 21
CHEST PLATE
SMALL AMOUNT OF AIR PRESENT ON ENTRY
SMALL AMOUNT RESIDUL PLEURAL THICKENING
RECTAL TEMP °F
104 103 102 101 100 99 98 97
RBC IN MILLIONS 3.7 2.7 6.2 4.8
HB IN GRAMS 12.0 15.5 12.0
WBC 12,000 10,600 10,800 7,350 13,600 15,000 11,000 9,500
BLOOD CULTURE NEG
THORACENTESES IN CC 110 180 30 100 50 20 0 0 0 30 20 4 15 2 0
SMEAR + + + + +
CULTURE + + + + – + – – – – –
PENICILLIN-I PLEURALLY 25,000 UNITS ONCE DAILY
PENICILLIN-SUBCUT. 10,000 UNITS q THREE HOURS
TRANSFUSIONS IN CC 200 300

Fig. 10: Empyema thoracis treated without surgical drainage.

Figures 9 and 10 illustrate two cases of empyema treated by non-surgical means. Both cases were treated by simultaneous systemic and intrapleural penicillin. Each day a thoracentesis was performed, as much pus as possible aspirated, and penicillin (in a solution of 1000 units per c.c. of saline) instilled. Although everyone does not agree on the advisability of this mode of therapy, it has been quite successful in our experience. It goes without saying that it can be used only in those cases in which the pus is accessible to aspiration and thin enough to pass through a needle of large caliber.

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SULFONAMIDES AND ANTIBIOTICS IN OTOLARYNGOLOGY

THE GENERAL PRINCIPLES OF THEIR USE

GERALD F. JOSEPH, M. D.†

BATON ROUGE

There is probably no field in medicine which has been more profoundly affected by the introduction of sulfa drugs and antibiotics than otolaryngology. The otolaryngologist, whose time was once almost fully occupied with the treatment of acute infectious complications of upper respiratory diseases, now finds a great deal of his time spent on allergic disorders, rhinoplastic procedures, surgery of the neck, and peroral endoscopy. The changing nature of otolaryngologic practice was the theme of a recent address by Coates[1] before the American Academy of Ophthalmology and Otolaryngology. Even more significant is the fact that the American Board of Otolaryngology is now urging candidates for certification to become proficient in endoscopy, allergic disorders and plastic surgery as well as the more conventional ear, nose and throat specialties.

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OTITIC DISEASE

Perhaps the most marked effect of changes in otolaryngologic practice as the result of new therapeutic methods is in the field of otology, in which the surgical treatment of acute mastoiditis and its complications has almost disappeared. Only occasionally today does the otologist see a patient with acute surgical mastoiditis in private practice, while in large public clinics hardly enough cases are seen for the young physicians to secure adequate training in surgery of the temporal bone. The situation is nationwide. It is especially noted in the South, however, where the milder climate has always kept the incidence of surgical mastoiditis comparatively low. On the very large otolaryngologic service at Charity Hospital of Louisiana at New Orleans mastoidectomy was once considered a surgical chore. Now the resident staff looks upon the operation as an unusual privilege.

The disappearance of surgical mastoiditis at this institution is statistically evident, and is out of proportion to changes in the hospital population. Over the 11 year period ending in 1946, a period during which sulfa drugs and antibiotics were introduced and popularized, the incidence has shown a steady decline (table 1). In 1936 there were 95 operations done for this condition. In 1946 only 13 were done. Furthermore, the rate of decline reflects almost directly the progress in development of these new therapeutic agents. Definite graphic plateaus indicate the introduction and use of each new group of drugs, though only after penicillin became available in adequate quantities did the drastic decline to the present low level occur.

Prior to the introduction and widespread use of penicillin there was a growing feeling that the sulfa drugs were beginning to fail. Streptococci are the principal causative micro-organisms in otitis media,[2] and sulfa-resistant strains were appearing. In-

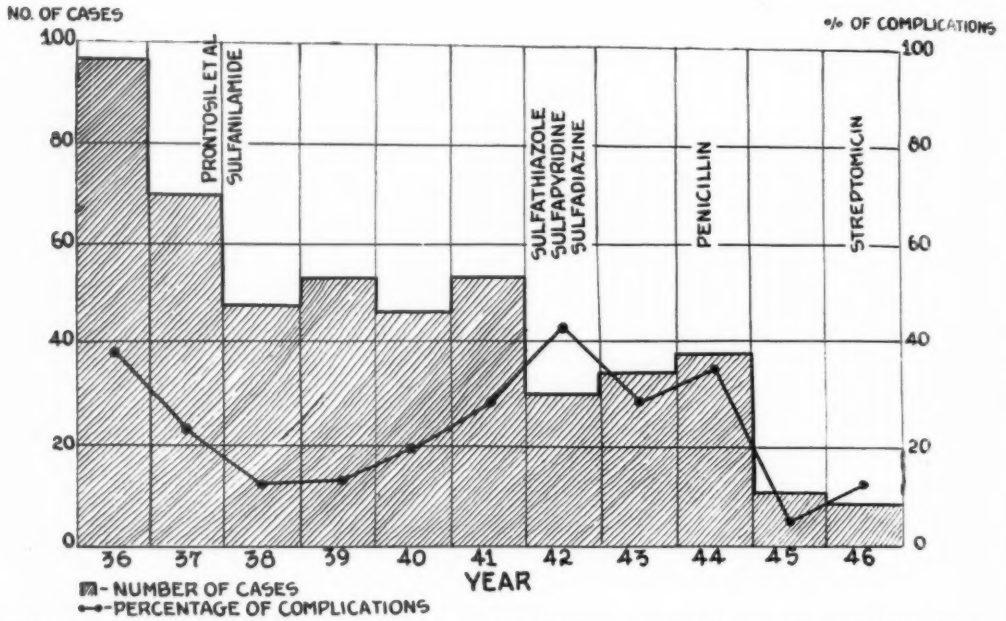

TABLE I: Showing the decrease in number of mastoidectomies done at Charity Hospital, New Orleans, during the eleven year period ending in 1946. Note the step-like decline in surgical mastoids with the introduction of each new group of drugs. Also note the tendency toward increase in percentage of complicated cases after each drug had been in use for a period of time.

stead of curing the otitic infection, in many cases the sulfa drugs were found to be masking symptoms.[3, 4] As a result, serious complications had often developed by the time it became evident that surgery was necessary.

An incident reported by von Christierson[5] in 1946 so well illustrates this point that it is worth repetition: During the winter of 1934-1944 a severe epidemic of streptococcic infections developed at a large Naval training station. A sulfa-prophylactic program was immediately begun and until midwinter the results seemed excellent. At that time it was observed independently by several medical officers that sulfa-therapy did not seem useful in numerous cases, and it became clear that sulfa-prophylaxis had been responsible for this development of sulfa-resistant organisms. One immediate result was an explosive increase in the incidence of surgical mastoiditis, in many cases associated with grave complications, which developed without being detected because septic symptoms were masked by sulfonamide therapy. By January 1945 the proportion of surgical mastoiditis among well supervised patients with otitis media was 26.5 per cent, and a quarter of the patients who developed mastoiditis had dangerous intra-cranial complications. This alarming situation continued until April, at which time adequate supplies of penicillin became available for the treatment of patients who did not respond to sulfa therapy. The effect was immediate. In May, only 6.5 per cent of the patients with otitis media required mastoidectomy, while only one patient with mastoiditis had any complications.

This is not an isolated instance. Numerous episodes of the same kind have been reported by other observers.[6, 7] Quite evidently although the sulfa drugs and antibiotics are invaluable in the prevention and treatment of middle ear infections, they do not furnish complete protection, and constant supervision and observation of the

patient are necessary, especially when a sulfonamide is used.

Up to this time neither penicillin nor streptomycin have been used for sufficiently long periods to permit definitive conclusions, but warnings are already appearing that penicillin, like the sulfonamides, can mask symptoms in otitis media[8, 9]. The rapidity with which certain pathogens can develop a resistance to antibiotics has been demonstrated in vitro by Miller and Bohnhoff,[10] who were able to produce strains of streptomycin-resistant meningococci by only two or three transfers into agar containing increasing concentrations of the antibiotic. Resistance to penicillin, while less rapidly developed, was also apparent after remarkably few transfers. Both clinical and experimental observations, in short, almost make one fear that lack of material at this time for training otolaryngologists in temporal bone surgery may be felt at some future date unless new antibiotics are constantly developed to keep ahead of the development of resistant pathogenic micro-organisms.

Chronic Middle Ear Infections: Chronic infections of the middle ear respond only equivocally to sulfa drugs and antibiotics. The best results have followed their local use. Kopetzky[11] reported some benefit from the use of a digesting mixture containing urea and sulfathiazole in a glycerine base, and there have been other isolated reports of good results from the introduction of penicillin-containing solutions into the middle ear under pressure or by means of Proetz displacement through the aural canal and Eustachian tube.[12] The best results, however, are not striking.

Collins and Hughes[13] probably have found the correct explanation of the poor results of these new drugs in chronic infections of the middle ear as their bacteriologic studies, show that the micro-organisms responsible for most cases of middle ear infection are not susceptible to either penicillin or the sulfonamides. Mixed infections are common, and for this reason it is important to make repeated bacterial checks in cases in which this form of therapy is used. It is quite possible for a gram-positive strain to be controlled while the role of invader is taken over by a gram-negative pathogen not previously detected. In the absence of serial smears and cultures such cases are frequently set down as therapeutic failures.

Two instructive cases were recently observed on the Charity Hospital service of the Louisiana State University School of Medicine. Both patients presented chronic otorrhea with acute exacerbations. All types of treatment, including the administration of a sulfonamide and penicillin by local and systemic routes, had been ineffective. One patient, a 7 year old child, had required mastoidectomy twice in the preceding year for subperiosteal abscess. After the last operation the wound had failed to close and three attempts at secondary repair had been unsuccessful. When a culture report was obtained, it showed a small growth of gram-positive cocci with swarming *Bacillus proteus*. Streptomycin used as frequent irrigations had the ear dry within one week and the wound went on to uncomplicated closure.

The second patient, an adult negro woman, had an acute flare-up of an old chronic otitis media. Although she showed some response to penicillin, she continued to run a low grade fever and to show some local signs of mastoiditis. Mastoidectomy was under consideration, on the basis that penicillin might be masking the development of complications, when a culture was reported showing overwhelming *Bacillus proteus* growth with a small element of gram-positive streptococci. As in the first case, streptomycin, in this instance by the intramuscular route, produced prompt results. Evidence of mastoiditis subsided rapidly and operation was not required; there has been no evidence of recurrence over a long period of observation in the outpatient clinic. It is probable that in both of these cases gram-positive cocci were originally present in large numbers but that, after penicillin therapy, *Bacillus proteus* assumed

the major role and continued unchecked until controlled by streptomycin.

Otitis Externa: This condition, while it responds well in some instances to sulfonamides and antibiotics, whether used locally or systemically,[8, 9, 14, 15] is not one of the diseases in which either the treatment or the outcome has been radically altered by their introduction. This is not true when the infection spreads beyond the ear canal and a cellulitis of the scalp or face develops or when a lymphadenitis or lymphangitis appears as a complication. In such cases the new forms of therapy are extremely effective. In the uncomplicated cases of so called otomycosis however, they are not of great value, probably because a gram-negative organism is so often the pathogen in these infections. In such cases streptomycin should be of great help when available in sufficient quantities.

PHARYNGEAL AND RELATED INFECTIONS

In acute infections of the pharynx and related areas excellent results can be expected from the use of the sulfonamides and penicillin. The regional blood supply is good, and medications administered systemically can readily reach the site of disease. Even the local use of these drugs, through the medium of pastilles or lozenges, should be useful. These expectations seem borne out by a number of early reports on their use in tonsillitis, peritonsillitis, and pharyngitis.[14, 15, 16, 19] Later, more careful analyses, on the other hand, suggest that the results may be less spectacular than was originally supposed. Spink[17] and his associates feel that the sulfonamides are of questionable value except in severe infections of the pharynx with toxic manifestations, and indicate that the rate of relapse after both sulfa therapy and penicillin is exceedingly high. Clodfelter,[18] in a well controlled study, noted that patients who had been given a sulfa drug had more rapid relief from symptoms of tonsillitis or pharyngitis but suffered from secondary rises in temperature and were ill longer than patients who were not thus treated.

Vincent's ulcer of the tonsils is one infection in this area which responds almost miraculously to small doses of penicillin.[21] Within a few hours after the intramuscular administration of as little as 25,000 Oxford units, the lesion has sometimes completely disappeared. To avoid relapse, however, it is recommended that treatment consist of two doses of 50,000 units each, at three hour intervals. Subsidence of symptoms occurs in most cases within four to six hours after treatment is begun, and practically always the lesion will completely disappear within a week without further care of any kind. This disease is a striking illustration of the value of the antibiotics when the causative lesion is highly susceptible to them.

Although promising results from the use of lozenges and pastilles containing sulfa drugs or penicillin are found in the literature,[22] doubt is expressed as to the actual value of this type of therapy, and it is not customary to rely upon these methods in the treatment of severe infections. Probably most patients, if not all, would fare just as well if lozenges and pastilles were omitted. It has been shown by McGregor and Long[20] that the salivary flow is such that a considerable amount of the contained drug may reach the tonsils from lozenges, but that the pharynx does not receive a sufficient salivary bath to be affected by a drug contained in a tablet held in the mouth. If the physician desires to use pastilles for pharyngeal disease, it is suggested that sufficient of the drug be contained in it to result in a detectable blood level from absorption in the alimentary tract.

LARYNGITIS

Penicillin and the sulfonamides are of value in acute infections of the larynx, just as in acute infections elsewhere, if the causative organisms are susceptible to these. This is particularly true of the types of acute laryngitis in children which results in croup and which may extend into the trachea in the form of laryngotracheobronchitis. When these patients require tracheotomy, instillation of a few cubic centimeters of salt solution containing penicillin into the tracheotomy tube every two or three hours serves to keep the bronchi

moist, controls local infections, and speeds recovery.

Aerosol penicillin[23] has been suggested as beneficial in acute laryngitis, but the drying effect of forced inspirations of air or oxygen may overbalance the benefit derived from the antibiotic. In tuberculosis of the larynx Figi's success[24] with intramuscular streptomycin has stimulated clinics all over the country to use the drug in this disease. It seems to give good results, but the rule still holds that the larynx will not remain healed unless the sputum becomes negative and the pulmonary lesion is arrested.

NASAL AND SINUS INFECTIONS

Penicillin and sulfa drugs have been used systemically and locally, with some success by both routes, in the treatment of infections of the nasal passages and the paranasal sinuses.[8, 9, 14, 15] It is reasonable to expect that they would benefit an acute hyperemic sinusitis if they were used systemically before the stage of suppuration. After empyema of the cavity develops, on the other hand, drainage by some means is necessary to effect a cure.[25] Definite improvement is likely to follow their use by lavage, by cannulization, or sinus puncture, or by the Proetz displacement method, but it is hard to evaluate their exact role. Simple drainage by lavage with saline solution will greatly benefit in most instances of sinus empyema, and the value of the addition of any bacteriostatic agent is questionable. Even in a diseased sinus the action of ciliated mucous membrane will quickly expel anything introduced into the cavity, while penicillin and the sulfonamides, to be effective, must remain in contact with the infectious organisms at least two or three hours. These drugs may be of some value if the sinus ostium is blocked, so that the drug used cannot escape, but the sinusitis, in that event, will not clear up until the occlusion is relieved. In other words, though the sulfonamides and antibiotics may be useful in sinus disease, certain factors limit their value and make their role in an ultimate favorable outcome at least doubtful.

The incorporation of antibiotics and sulfa drugs into nose drops has achieved popularity in recent years, and at the present time many commercial preparations are available which combine these agents with a vasoconstrictor. The value of such preparations is questionable, for nose drops do not remain in contact with the inflamed nasal surfaces long enough for them to be effective.[25, 26, 27] Penicillin in weak solutions is known to be harmless to the nasal mucosa,[26] and its use, aside from possible unpleasant local sensitivity reactions, is not objectionable. The same cannot be said of the sulfonamides. A number of commercial preparations containing soluble sodium salts of sulfonamides are highly alkaline and they exert a caustic effect in the nose[28] which is destructive to the nasal mucosa and correspondingly harmful to the patient. Any nose drops with a pH over 6 are to be avoided.[27, 29]

In chronic sinusitis, which is often the result of an individual allergic response or of poor mechanical drainage to the infected sinus, antibacterial agents have proved of little value. A chronic infection may be helped during an acute exacerbation by the systemic administration of penicillin or sulfa drugs, but it cannot be said that their use improves the patient's chances for ultimate cure of the chronic state, in which carefully planned surgery and desensitization therapy are the most likely roads to relief.[27] In this condition, just as in chronic otorrhea, the explanation is undoubtedly the presence of nonsusceptible pathogens.

Although promising results have been reported from the use of areosol penicillin in the treatment of sinus infections,[23] this is another condition in which it is questionable whether the means of administration has much to do with the benefits observed. The blood level achieved by absorption of the drug in the pulmonary alveoli must be credited with any good results. It was shown long ago[29] that air passing through the nose does not enter the sinuses, while the volume of air exchanged between the sinuses and the nasal passages is minute. Proetz has estimated that it requires many hours for a single complete change in the

air content of a sinus to occur as the result of the respiratory motion of nasal air. Studies are now being conducted at the Columbia University College of Physicians and Surgeons in the treatment of sinus disease with aerosol penicillin by means of an alternating positive and negative pressure apparatus. There are obvious dangers inherent in such a method, but it offers a rational approach to the problem, and it may prove very valuable.

BRONCHOPULMONARY INFECTIONS

The otolaryngologist whose practice includes bronchoesophagology has found penicillin and the sulfa drugs useful in this field.[30] The intrabronchial instillation of penicillin solutions (as well as of streptomycin) through the bronchoscope in the treatment of chronic bronchopulmonary infections such as lung abscess and bronchiectasis has met with great success. Sulfa drugs, in the form of powders, have been insufflated into the respiratory passages by the same route, but caking of the powder has been reported and the method is obviously undesirable. Antibiotic aerosols find their greatest usefullness in this type of infection. They have been utilized for both palliation and cure, as well as in preparation for thoracic surgery, and the results have been almost uniformly favorable.

PENICILLIN BY THE ORAL ROUTE

In the opinion of many observers penicillin by the oral route should be more useful in otolaryngology than in many other fields of medicine. A large proportion of patients with otolaryngologic disorders are not seriously ill and can remain ambulatory. For these reasons, in spite of the variable results to be expected, oral administration of penicillin seems justified. Some reports are distinctly encouraging, and Lierle's[31] experimental studies have put the method on a logical basis. The blood levels produced by oral administration are usually adequate to control simple infections and prevent complications, and if the patient is kept under close observation, there can be no objection to the method on the ground of safety. The use of Romansky's beeswax and oil formula[32] is more logical, but many patients object to injections by needle for conditions which are not disabling.

DISCUSSION

It probably seems somewhat confusing for a communication which began with the statement that the sulfa drugs and antibiotics have materially altered the practice of otolaryngology to be chiefly concerned with a discussion of the limited effectiveness of these agents in the common infections of the ear, nose and throat. Some comment is obviously needed to clarify the situation.

It should be noted first of all that most of this presentation has had to do with the use of chemotherapy and antibiotic therapy in such simple infections as tonsillitis, sinusitis, laryngitis and pharyngitis, all of which may be termed "office practice" diseases. In these conditions the value of the new methods is still under debate. The literature is confusing, and my purpose in this communication has merely been to analyze it and edit it, so to speak, for the benefit of those who are not otolaryngologists.

In the prevention and treatment of the serious complications which may result from such minor infections as those mentioned, there is no doubt of the value of these new agents. They are extremely useful. The control of mastoiditis from otitis media is an outstanding example of their value. Extension to the mastoid air cells and adjoining regions still occurs in spite of their use, when the causative microorganisms are drug-resistant, but on the whole, mastoiditis is now a waning disease, intra-cranial complications are relatively infrequent, and their lethality has been greatly reduced. Meningitis, cerebral abscess, lateral sinus thrombosis and petrositis can usually be cured by the use of the antibiotics or sulfonamides, combined, if necessary, with appropriate drainage. Osteomyelitis of the frontal bone, and cavernous sinus thrombosis, which formerly were dreaded complications because of the high mortality associated with them, now usually can be prevented or, if they occur, can often be cured by the use of these new remedies. Hill,[33] in his recent appraisal

of Mosher's "seven great problems in otolaryngology", listed them as among the problems which are approaching solution. What is true of mastoiditis is also true of all soft tissue and intracranial complications of infections of the ear, nose and throat. They are usually preventable by the early use of the sulfa drugs and antibiotics and if they develop, they can usually be cured, often without surgical drainage, by use of the same agent. It is therefore fair to say that otolaryngology is a different specialty today from what it was 10 years ago.

SUMMARY

1. The advantages and limitations of the sulfonamides and antibiotics have been discussed in relation to various otolaryngologic conditions.

2. The limited usefulness of these agents in the so-called "office practice" diseases has been pointed out, and their extreme value in serious complications which may result from these minor infections has been emphasized.

3. The risk that sulfonamides and antibiotics may permit serious complications to develop by masking symptoms in mastoiditis must be borne in mind by every physician who uses them.

4. In spite of the fact that these new agents are not "cure-alls" they have completely altered the character of otolaryngologic practice, and when properly employed, they have an enormous prophylactic and therapeutic field of usefulness.

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ADULT HYPOTHYROIDISM AND MYXEDEMA

A REVIEW OF THE DIAGNOSTIC DATA IN 151 CASES

NORMAN BURNSTEIN, M. D.†

NEW ORLEANS

In this study the inclusive term adult hypothyroidism is applied to all cases of hypometabolism believed to be due to a decrease of thyroid hormone; hypothyroidism of severe degree characterized by marked reduction of the basal metabolic rate and the classic clinical features of severe hypothyroidism are here classified as myxedema.

TOTAL INCIDENCE

In the 11 year period from 1935 through 1945, a total of 151 cases of adult hypothyroidism and myxedema were admitted to the Charity Hospital. During this period the total number of admissions to the hospital, exclusive of newborns, was 553,240; the incidence of hypothyroidism was thus 0.0002 per cent. Of the 151 patients, 43, or 22 per cent, had frank myxedema. Reports from institutions in other parts of the United States give a higher incidence than the figures noted here. Means[1] noted that at the Massachusetts General Hospital patients with myxedema constituted 0.08 per cent of the total number admitted to the wards. Shepardson and Wever[2] found an incidence of 0.04 per cent of admissions in the University of California Hospital in 1934, and at the Mayo Clinic[1] in 1935 patients with myxedema constituted 0.07 per cent of total hospitalized patients.

RACE

Of the 151 cases, 111 occurred in white persons and 40 in negroes, during a period when 283,516 whites and 269,724 negroes were admitted to the hospital. Hypothyroidism was thus about three times as common in persons of the white race. Of the cases of myxedema, 35 were in whites and eight in negroes. A survey of the literature did not reveal data regarding the comparative incidence of hypothyroidism in the white and negro races.

SEX

One hundred and thirty-one of the 151 patients, or 86 per cent, were females. Thirty-one of the 43 cases of myxedema, or 72 per cent, occurred in females. Means[1] in studies at the Massachusetts General Hospital found an incidence of 82 per cent in females in cases of myxedema. Kohlhas[3] found a ratio of 10 males to 40 females, and Thompson[4] found similar results in his report.

AGE

The age incidence is listed in table 1, which shows that half of the cases occurred in individuals below the age of 40, and 40 per cent below the age of 30. Kohlhas[3] found the average age in 50 cases studied to be 34 years. Thompson[4] states that the disease occurs more frequently in the fourth, fifth, and sixth decades of life.

TABLE 1

AGE INCIDENCE

Age	Number of Cases: Hypothyroid	Myxedema
18 - 30	46	15
30 - 40	31	6
40 - 50	17	6
50 - 60	10	8
Above 60	4	8

PRESENTING SYMPTOMS

In table 2 the complaints of these patients and their frequency of occurrence are listed. The onset of the symptoms was slow in all cases; in 10 cases symptoms were first noted during or shortly after pregnancy. The presenting complaints were most frequently referable to the genital, gastrointestinal, neuromuscular, and cardiovascular systems. Symptoms of greatest frequency in myxedema were headaches, constipation, fatigue, backache, abdominal pains, and general body aches and pains. Lerman[5] in 1933, in a review of 77 cases of myxedema, noted similar findings in the symptomatology of myxedema. The above findings are in agreement with the findings of Rose,[6] Reilly,[7] and Pullen[8] that the presenting symptoms in cases of mild and moderate hypothyroidism may be manifold and nonspecific.

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TABLE 2

SYMPTOMATOLOGY

Symptoms	Hypothyroidism Cases Number	Per cent	Myxedema Cases Number	Per cent
Irregular menses	33	32	3	7
Abdominal pains	31	28	11	26
Headaches	26	24	15	35
Anorexia	23	21	5	12
Nausea	21	20	9	21
Increased menses	18	17	2	5
Fatigue	17	16	19	44
Weight loss	15	15	7	16
Constipation	16	15	17	40
Backache	16	15	13	30
Nervousness	14	13	4	9
Weight gain	15	14	7	16
Vomiting	15	14	5	12
Cardiac pains	14	13	10	23
Lethargy	13	12	6	14
Qualitative dyspepsia	11	10	4	9
Cardiac palpitations	10	10	5	12
Epigastric fullness	9	8	6	14
General aches and pains	9	8	10	23
Dizziness	8	7	7	16
General malaise	8	7	5	12
Amenorrhea	8	7	2	5
Memory impairment	7	6	7	16
Decreased menses	7	6	0	0
Sensitivity to cold	6	4	7	16
Increased lacrimation	6	4	3	7
Dyspnea	5	4	1	3
Sleepiness	4	3	3	7
Diarrhea	2	2	7	16
Earache	3	2	0	0

PHYSICAL SIGNS

The physical signs believed to be associated with the hypothyroid state are listed in table 3. The findings stress the fact that physical findings of a characteristic nature are much more frequently found in the cases of myxedema than in varying lesser degrees of hypothyroidism.

OTHER DISEASES

In the cases of hypothyroidism without frank myxedema, 53 per cent of the patients had other diseases which contributed importantly to the clinical picture, the most frequent being gynecologic disorders and gallbladder disease. On the other hand, only 18 per cent of the patients with frank myxedema had other significant disorders. Table 4 lists in order of frequency the primary diagnosis recorded.

LABORATORY DATA

The basal metabolic rates prior to the institution of replacement therapy are listed in table 5. Seventy-seven per cent of the patients with frank myxedema showed B.M.R. readings more than 20 per cent below normal.

TABLE 3

PHYSICAL SIGNS

Physical Signs	Per cent of Cases: Hypothyroid	Myxedema
Obesity	37	14
Enlarged thyroid gland	24	5
Hypotension	15	14
Cardiac enlargement	10	11
Coarse dry hair	10	5
Myxedematous facies	8	22
Edema of eyelids	8	21
Dry skin	8	37
Edema of face	7	37
Thick skin	4	16
Edema of hands	3	19
Thick tongue	3	14
Loss of body hair	3	16
Thin eyebrows	3	10
Coarse rough skin	2	10
Brittle nails	1	0
Cool skin	1	2
Fallid skin	0	9

TABLE 4

DIAGNOSES

Primary Diagnosis	Number of Cases: Hypothyroidism	Myxedema
Hypothyroidism or myxedema	58	35
Gynecologic disorders	20	1
Nephritis	3	2
Cholecystitis	7	0
Goiter, non-toxic	6	1
Postoperative thyroidectomy	6	2
Tuberculosis	2	0
Diabetes mellitus	1	1
Hookworm disease	0	1

TABLE 5

DISTRIBUTION OF BASAL METABOLIC RATES

Basal Metabolic Rate	Per cent of Cases: Hypothyroidism	Myxedema
—5 to —10	17	0
—10 to —20	29	7
—20 to —30	14	23
—30 and below	0.9	54
Not recorded	39	16

Blood cholesterol values were capricious in this series, probably because the method used for this determination was not reliable. In almost half of the 21 cases of myxedema in which blood cholesterol was determined, the level was below 200 mg./100 c.c.

The results of blood counts are shown in

table 6. In 42 per cent of the cases of frank myxedema, significant anemia was present. Six cases of myxedema showed a hyperchromic macrocytic type of anemia.

Electrocardiographic abnormalities compatible with or suggestive of hypothyroidism (low complexes, isoelectric T waves, prolonged QT interval) were noted in four cases of hypothyroidism and 14 cases of myxedema.

TABLE 6

	Per cent of Cases: Hypothyroidism	Myxedema
Total red blood cell count		
Above 3.5 million	23	23
Below 3.5 million	9	42
Hemoglobin		
Above 10.5 gm.	9	42
Below 10.5 gm.	23	20

SUMMARY

1. A study of 151 hospitalized cases of hypothyroidism and myxedema occurring in an 11 year period at a large Southern hospital are reviewed.

2. The relatively low incidence of these disease states in this region of the country is noted in contrast to much higher figures elsewhere.

3. The higher incidence of occurrence in the white race than in the negro race is emphasized.

4. The cases studied here occurred at an earlier age than in some other series.

5. Females had the disease more often than males, in general agreement with the finding of others.

6. Typical signs, symptoms, and laboratory data lend further emphasis to the general findings recorded in the literature.

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HUMAN ISOIMMUNIZATION

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NEW ORLEANS

Some of the clinical phenomena of heteroimmunization were observed as early as 1667 following the repeated transfusion of sheep blood into human recipients. The French surgeon, Denys, wrote of a patient, who, following a second such transfusion, exhibited a rapid pulse, nausea, profuse sweating and pain in the kidney region, followed the next day by passage of urine described as "black".[1] These are recognized as signs and symptoms resulting from the transfusion of incompatible blood and it is known that antibodies in the patient's blood initiate the unfavorable response by hemolyzing the transfused red cells, the black urine arising from the presence of hemoglobin pigments derived from the laked erythrocytes.

Here was an example of the sensitization of one species by an antigen present in a different one. This is relatively easy to demonstrate in laboratory animals and is the basis of preparing typing fluids for the identification of the M and N factors in human blood.

Isoimmunization, or sensitization within a species, was first described by Ehrlich and Morgenroth in 1900. By cross-transfusions between goats, they were able to demonstrate the development of immune antibodies in the recipients. The antibodies served to differentiate the bloods of individuals belonging to the same species. Applying the same methods, as *in vitro* procedures, Landsteiner[2] demonstrated in humans the existence of the normal isohemagglutinins anti-A and anti-B and established the identity of the four major blood groups, A, B, AB and O. This discovery stands as a genuine epoch in science because it not only made possible safe blood transfusion therapy, but also serves as the basis of all our

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accumulated knowledge of human isoimmunization.

Sensitization to the Rh factor of Landsteiner and Wiener is the best known example of isoimmunization in man and is recognized as the etiologic agent in some 92 per cent of all cases of hemolytic disease of the newborn and of intra-group hemolytic transfusion reactions.[3] Investigations in this field have also served to redirect attention to the presence of several different agglutinogens in human erythrocytes. Nearly all of the factors identified to date have been known to behave as antigens, albeit rarely in the case of some of them. The rare, and at times obscure, sensitizations deserve some consideration because they are concerned in the 8 per cent of cases of hemolytic disease and transfusion reactions not due to Rh.

The major group specific substances, A and B, are not confined to the erythrocytes but are present in almost every internal organ, especially glandular tissue. A large majority of individuals, apparently as an hereditary trait, also secrete their group specific substance in saliva, gastric juice and amniotic and other body fluids. Characteristic of the A-B groups is the presence of the normal isohemagglutinins, anti-A and anti-B, in plasma or serum. These are globulins and can be demonstrated in high protein body fluids such as milk, lymph and transudates.

The higher incidence of abortions and miscarriages in group incompatible matings was noted two decades ago and re-emphasized in recent years.[3, 4] In view of the many instances in which mother and fetus are group incompatible one would expect a considerable incidence of hemolytic disease due to differences in major group. That such is not the case is due to the fact that a majority of unborn infants secrete their group specific substance and the presence of this in amniotic fluid and fetal circulation serves as a protective mechanism by neutralizing or absorbing the antagonistic maternal isohemagglutinins. Thus, in the 8 per cent of erythroblastosis in offspring of Rh+ mothers, not more than 2 per cent probably are due to A or B hyperimmunization. These cases, when seen, however, are clinically indistinguishable from those caused by typical Rh sensitization of Rh— mothers.

Recently I reported such a case in which the affected infant and mother were both Rh+ , the baby belonging to group B and the mother to Group O, with the significant findings of a marked specific increase in maternal anti-B agglutinin and a negative test for B substance in the neonatal serum.[5] Unlike A and B, these agglutinogens are confined almost entirely to the erythrocytes and natural isohemagglutinins are very rarely encountered, while transfusion isoimmunization to M or N is but slightly more frequent.[9] These factors are identified by means of heteroimmune sera prepared from animals immunized to human M+ and N+ bloods.

M and N, like A and B, are inherited as simple Mendelian dominants, but unlike A and B, are never both absent. There are, then, three types of MN bloods in humans: M,N, MN. While subvarieties of the A factor are well known, such is not the case for M and N, although a subtype of N has been described.

The relationship of M and N is important in itself and further serves as a useful analogy in appreciating the reciprocal kinship between the Rh and Hr factors.

In 1928 Landsteiner and Levine[6] made an important contribution when they discovered yet another agglutinable factor in human erythrocytes. This agglutinogen, named P, apparently is confined to the erythrocytes and natural human anti-P agglutinins are extremely rare, although the sera of horses and pigs often exhibit agglutinins specific for the factor. It is inherited as a simple Mendelian dominant and the existence of subtypes has been suggested. On infrequent occasions the P factor behaves in an antigenic manner and a recent case of P isoimmunization was reported by Wiener and Unger in 1944.[8]

The complex or mosaic nature of the Rh factor is presently well verified. Essentially it consists of three subfactors designated Rh_0, Rh′ and Rh″.[10] Each of these is capable

of antigenic behavior following entrance into the circulation of an individual lacking it. The identity of the subfactors was established by the discoveries of human isoimmune anti-Rh sera giving respectively 85, 70 and 30 per cent positive reactions against erythrocytes of white individuals in general. Just as the three Rh agglutinogens co-exist in various combinations, determining the eight major subtypes, so the three Rh antibodies may be and are found singly or variously together in the serum of an isoimmunized person.

As Levine has repeatedly and so clearly shown, the anti-Rh_0 (85 per cent) serum is clinically of greatest value. The existence of the Rh subtypes explains some of the rare cases of erythroblastosis in infants of Rh+ mothers. In these instances the father and affected baby possess a subfactor absent from the blood of the mother, although she may possess both of the others. Intermediate Rh subfactors have been encountered, but to date constitute a rarity.

Originally it was believed that Rh was confined to the erythrocytes and was not secreted. However, the presence of Rh agglutinogens in certain organs and in saliva, gastric juice and amniotic fluids of Rh+ individuals has been demonstrated in a small number of cases. [11, 12] Secretion of Rh substance serves as one explanation of the occasionally normal Rh+ infant born to an isoimmunized Rh— mother. Further, this information brings within the realms of probability the development of a non-antigenic means of neutralizing Rh antibodies *in vivo*, a procedure which should cause a marked decrease in neonatal morbidity and mortality due to hemolytic disease of the newborn.

In 1941 Levine began the long series of studies which lead to our present extensive knowledge of the Hr factor.[3] In the early stages of this investigation, involving erythroblastosis in infants of Rh+ mothers, he established the existence of an agglutinogen bearing a reciprocal relationship to Rh and to it gave the apt name, Hr. More recent work by Levine and others has established the complex nature of Hr and the presence of three Hr agglutinogens Hr, Hr′ and Hr″, each corresponding to a respective Rh factor. In other words, a blood which is Rh— is Hr+. Further, the red cells of some people contain both Rh and Hr agglutinogens and some contain only Hr, the latter being the so-called "true" or "complete" Rh negatives. Levine was first to point out the analogy of Rh and Hr to M and N. Thus three MN types are possible: M,N, MN, types M and N being homozygous. Similarly three Rh-Hr types are possible, Rr, Hr and RhHr. Some bloods are homozygous for Rh (RhRh), some likewise for Hr (HrHr) while many individuals possess both factors and are therefore heterozygous (RhHr).

Hr is as highly antigenic as Rh, but few cases of Hr isoimmunization are seen due to the high incidence of heterozygous (RhHr) people. In a case of erythroblastosis still being studied, we found the father, two older children and the affected infant were all Rh+ Hr+ (thus heterozygous) while the mother was found to be Rh+ Hr— (thus homozygous for Rh) and to exhibit anti-Hr antibodies in her serum. Levine's general rule applied in this case, to wit: "the fetus must be heterozygous for the factor to which the mother is isoimmunized."

Actually we have only touched upon the subject of human agglutinogens and isoimmunization. A number of other factors have been identified in human blood but thus far seem of no clinical significance. It must be remembered that not all of these substances and their sub-forms are present in the erythrocytes of any one individual so that the possible permutations and combinations are almost infinite and from the original four major groups of Landsteiner we have progressed to identification of several hundred types of human blood.

CONCLUSION

This general statement may be made regarding human isoimmunization: Certain agglutinogens present in human erythrocytes at times behave as antigens, some to a greater degree than others; transfer of antigen takes place by blood transfusion

and or pregnancy, the erythrocytes of the donor (fetus) possessing one or more agglutinogens absent from the erythrocytes of the recipient (mother).

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NEW METHOD OF TREATING PEPTIC ULCERS WITH PENICILLIN GASTRIC DRIP

PRELIMINARY REPORT*

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The purpose of this paper is to bring before the staff members of this hospital the striking results obtained in treating four cases of proved peptic ulcers by a continuous gastric drip of penicillin in soda water for ten days.

I fully realize that the reporting of four cases is of little or no statistical value; however, the results were so striking that I feel justified in making this report.

As far as I can ascertain, this method of treating peptic ulcers with penicillin gastric drip has never been reported, and inasmuch as it is simple and of no danger to the patient it is worthy of extensive use in this type of disease.

The treatment is based on the theory that gastric ulcers are infected and the irritating factors of the stomach, namely, food and acid, interfere with the opportunity to heal. Therefore, the reasoning behind this method is simple. Remove the irritating factors and apply directly to the ulcer some non-irritating and non-toxic antibacterial agent. This we have in penicillin dissolved in soda water.

The method I have used on these cases was definitely to establish the exact location of the ulcer by fluoroscopy and x-ray. A small soft stomach tube was passed into the stomach via the nose and fixed in position so the stomach end is above the ulcer. The outside end is attached to a 1000 c.c. drip bottle suspended from an infusion stand and containing 200,000 units of penicillin dissolved in 1000 c.c. of tap water to which have been added two teaspoonfuls of bicarbonate of soda. This is regulated to drip continuously at the rate of 60 drops a minute. In all cases it was continued night and day for eight to ten days. The patient is not allowed to take anything by mouth except small sips of water to keep the throat moist, this only when absolutely necessary. Infusions of 5 per cent glucose in 1000 c.c. of normal saline are given once each day. Codeine and luminal by hypodermic were used occasionally at night to insure adequate rest. Nothing else was given the patient.

The criteria used to know when to remove the tube were daily gastric analysis, symptomatic relief, and, finally, fluoroscopy and x-ray demonstrating absence of the ulcer.

CASE NO. 1

Mr. M. C., aged 42, was admitted to the hospital on June 3, 1946, with a history of pain in the epigastrium accompanied by nausea and vomiting. Patient stated that he had been under treatment for stomach ulcer for over a year. X-ray diagnosis was made and he had been on a diet ever since with very little relief. Two days before admission he began to suffer severely from pain and nausea which had become unbearable. Vomiting was clear, very acid, no blood.

Physical examination revealed a well nourished

*Read before the staff of the Baton Rouge General Hospital July 16, 1947.

white male whose weight was 150 pounds, not acutely ill. The head was negative; chest negative; lungs clear; heart normal. B. P. 140/90. Abdomen was soft. There was a marked tenderness over epigastric region extending down to the umbilical region; genitalia and extremities normal.

X-ray and fluoroscopic examination: On the posterior wall of the pyloric canal is a residual fleck which is persistently observed when the barium is partially expressed. There is localized tenderness over the area. The fleck is believed to represent the crater of an active gastric ulcer.

Laboratory: Gastric analysis: Total acidity 70; HCl free 60. Blood: Kahn and Wassermann negative. Red blood cells 4,050,000; white blood cells 5950; hemoglobin 75 per cent; S. L. 41; L. M. 5; F. N. 53; E. 1; negative malaria; urine negative; temperature normal.

Treatment: Using soft stomach tube, via nose, the penicillin gastric drip was started June 10, 1946, with 1000 c.c. tap water, two teaspoonfuls of bicarbonate of soda with 200,000 units of penicillin. A continuous drip, 60 drops per minute, continued for eight days. An infusion of 1000 c.c. of 5 per cent dextrose was given once daily.

Progress: Daily gastric analysis showed absence of free HCl with a total acidity averaging 15 per cent. There was relief of symptoms on the third day; no complaints; no hunger or thirst experienced by patient. The bowels moved daily without aid. On the morning of the ninth day the tube was removed and an x-ray made.

X-ray and fluoroscopic examination, June 18, 1946: No evidence of fleck. Slight angulation at pyloric-duodenal junction is attributed to scarring results from the healed ulcer. Patient was placed on a full diet with no return of symptoms.

Follow-up: Twelve months after discharge the patient had gained 40 pounds, had no symptoms, and stated he could eat anything he wishes without and symptoms or discomfort.

CASE NO. 2

Mr. M. C., aged 23, was admitted to the hospital on May 27, 1947 with a chief complaint of pain in the stomach, gnawing in character, relieved for a short time by drinking milk. He was unable to eat any solid food because of nausea. Had x-ray diagnosis of duodenal ulcer prior to admission. Examination revealed a white male not acutely ill, underweight, and extremely nervous. Head normal; chest normal; abdomen, marked tenderness in region of epigastrium; extremities and genitalia normal.

X-ray report on June 7, 1947: Findings reveal large fleck in first portion of the duodenum which did not disappear on pressure, and tenderness was elicited on palpation. Diagnosis: duodenal ulcer, moderate size.

Laboratory: Gastric analysis: Not reported from laboratory prior to treatment. Red blood cells 5,650,000; white blood cells 9,000; hemoglobin 90 per cent; S. L. 19; P. N. 80; E 1; negative malaria.

Treatment: Continuous penicillin gastric drip as described above was carried out for 10 days; one infusion daily of 5 per cent glucose, 1000 c.c. given.

Progress: On third day, complete relief of all symptoms was reported by the patient. Gastric analysis was reported free from HCl, total acidity of 5 on the third, sixth and eighth days. During treatment the bowels moved normally, no hunger or thirst experienced. Tube was removed on the morning of the eleventh day and x-ray and fluoroscopy made immediately after. Report: The findings revealed complete healing of the moderate size ulcer crater previously described with a slight cicatrization as a residuum.

The patient was placed on a full diet and, having no discomfort or symptoms, released from the hospital. A check-up on the case at time of reading of this paper. He states that he is eating anything he wants and has no discomfort, and he is working full time without fatigue.

CASE NO. 3

Mrs. D. T., aged 59, a white female gave a history of pain in the stomach for past 12 months, accompanied by nausea and occasional vomiting. She has had almost constant pain in stomach for past three months and she has been unable to eat anything except milk and cream; she has been very irritable and nervous. Patient stated that she was diagnosed duodenal ulcer by x-ray and admitted to a New Orleans hospital for six weeks, at which time she was given milk and cream and amphojel. She was relieved and came home three months ago. Since being home, a return of the symptoms occurred with a gradual increase in the severity. The day prior to admission she vomited a small amount of blood.

Physical examination: Well nourished white female, not acutely ill. Head normal; chest normal; lungs clear; heart normal; B. P. 148/84, pulse 80; temperature normal. Abdomen: no scars, marked tenderness of the epigastrum on slight pressure, no masses felt, liver and spleen not palpable; extremities normal.

X-ray and fluoroscopy: The duodenal cap exhibits a marked filling defect, indicating an ulcer of the first portion of duodenum. Six hours after the barium meal there is a retention of barium in the ulcer crater.

Laboratory: Gastric analysis: Total acidity 80, free HCl 60; urine, negative except for faint trace of albumin. Blood: white cells 7,150; S. L. 37; L. M. 3; P. N. 60; no plasmodia found.

Treatment: Penicillin gastric drip continuous for 10 days as previously described.

Progress: Complete relief of symptoms occurred on the third day. Patient tolerated the treatment well; bowels moved well throughout treatment, and after the fourth day she walked out on the sun porch daily, carrying her drip bottle which

she would hang up on an infusion stand and she would sit in a chair for two hours. She did not require any sedation at night to rest. Her daily gastric analysis revealed no free HCl and average total acidity of 15 units each day throughout the 10 days. Tube was removed on the eleventh day and x-ray and fluoroscopic report was as follows: There is evidence of a healed ulcer of the duodenum. On emptying, no fleck remains. This patient was placed on a full diet and thus far no discomfort or symptoms have occurred.

CASE NO. 4

Mr. P. E. E., a white male, aged 51, was admitted to the hospital June 14, 1947, with a chief complaint of pain in the stomach of a burning character; nausea and eructation of very acid fluid, inability to eat anything without considerable pain and nausea. The symptoms began three months ago. Prior to that time he suffered quite a bit with indigestion. Has become very nervous and irritable. Past history is negative.

Physical examination revealed a white male, well nourished, not acutely ill, approximate weight 170. Head normal; chest normal; lungs clear; heart normal. B. P. 130/80. Abdomen: marked tenderness in epigastrium on palpation, no rigidity, no masses, liver and spleen not palpable. Genitalia and extremities normal.

X-ray and fluoroscopic examination: A moderately large fleck in the first portion of duodenum, persistent on compression, and marked tenderness on pressure. Diagnosis: active duodenal ulcer.

Laboratory: Gastric analysis: Total acidity 70, free HCl 55. Blood: red blood cells 5,700,000; hemoglobin 90 per cent; white blood cells 8,000; S. L. 26; L. L. 4; P. N. 69; E 1; negative malaria. Urine negative. Blood Wassermann negative.

Treatment: Penicillin gastric drip continuously for ten days as described above.

Progress: Complete relief of symptoms occurred on the fourth day. Daily gastric analyses showed a gradual decline the first three days to total acidity of 4, no free HCl. This remained low for an average of 4 to 6 total acidity, no free HCl. The treatment was tolerated well and bowels moved regularly after the second day. The tube was removed on the morning of the eleventh day. Immediate x-ray and fluoroscopic examination was made.

Report: No fleck visible. No tenderness noted by patient. Examination of the patient in both the erect and dorsal decubitus, with and without compression, fails to reveal the ulcer which was observed June 11, 1947. The findings suggest complete healing of the previously described large duodenal ulcer. The patient was placed on a full diet with no complaints or discomfort.

Follow-up at the time of reading of this paper: Patient stated he could eat anything and had no symptoms, that he was the happiest man in town. No tenderness could be elicited on examination of abdomen.

CONCLUSION

I would like to emphasize again that this short series of cases in this preliminary report are not conclusive evidence by any means that this form of therapy is the last word, but the striking results warrant further investigation along these lines.

I hope that each member of the staff here tonight will feel free to discuss and criticize this therapy as he sees fit.

In conclusions I would like to thank Dr. Arthur Alexander and Dr. Lester Williams, radiologists, for their splendid help and cooperation with these cases, and Dr. Brinsfield King and Dr. Jack Bevens, pathologists, for their diligent cooperation.

DISCUSSION

Dr. C. H. Mosely: Do you feel that patients get well quicker with this treatment than with amphojel or milk?

Answer: It is my impression that an ulcer is infected although there are different schools of thought on this. All I can say until more time goes by is that the patient gets well quicker with this treatment. I believe a patient could stand the treatment over ten days. However, this has been sufficient to complete healing in these four cases.

Dr. G. H. Riche, Jr.: Did you give the patients any sedation?

Answer: To the first patient, I gave codeine for first three days, but after that he did not need any. The third patient was given luminal twice the first two days after which she slept all night without any sedation.

Dr. J. D. Martin: Do you think that simply putting the patient to bed where he could get the proper rest and diet and could be removed from his environment would cure the patient as well?

Answer: Perhaps, but the time limit would be longer, while this treatment is short. The lady who stayed in a hospital six weeks on an amphojel and milk diet was cured in ten days with this treatment.

Dr. J. E. Toups: I would like to request that in the next case treated the penicillin be left out.

Answer: In the third case, as soon as acid disappeared on third day, I stopped the soda and gave pure penicillin and tap water. In the fourth case, soda was cut to 1 dram instead of 2.

Dr. R. B. Wallace: Do you think there is secondary infection around an ulcer?

Answer: That is the theory on which this treatment is based. Heretofore, the stumbling block has been acid in the stomach, which is the reason for using soda in order to neutralize the acid to the point where penicillin will be effective. It is well known that the antibacterial effect of penicillin

is destroyed by HCl in stomach, thus the soda bicarb. is used.

Dr. G. H. Riche, Sr.; Has the first patient been followed up?

Answer: Yes, for one year, with no symptoms or discomfort. The other patients have also been followed up, for a shorter period, of course. None has had a return of symptoms.

Dr. L. H. Stander: Because of the high incidence of malignancy, I should like to advise caution in the treatment of gastric ulcers in the stomach proper as it is a well known fact that gastric carcinoma does ulcerate. Early surgery for gastric ulcers would be the most proper form of therapy because of the high incidence of carcinoma of this type.

Answer: I fully agree with Dr. Stander's statement. Caution should be exercised in treating ulcers in the stomach by this method. During this series of cases I had a case of just such a circumstance. The stomach ulcer was large and of long standing. It was elected to do surgery and he was referred to the surgeon. A partial gastrectomy was done. The resected ulcer did not show any malignancy on section. In this particular case I feel now that the penicillin gastric drip would have been effective. Ten days more would not have harmed the patient any, and if a complete healing did not occur, operation could then have been undertaken.

FOLLOW UP NOTE: Since this paper was read July 16, 1947, 24 patients have been treated. Of the 24, 21 have been cured and three were failures. Of the three, one case passed kidney stones on the third day of treatment and it was necessary to discontinue treatment. The second patient became nervous and would not tolerate the tube in his stomach. The third patient developed penicillin rash on the third day of treatment. He was continued on the drip for five more days without penicillin, simply using a soda water. This was discontinued because of pain in the stomach and nausea. X-ray showed that there was no healing of the ulcer and indicated that soda water drip itself is not beneficial, answering in a way the question asked by Dr. J. E. Toups during the discussion.

—o—

THE USE OF CURARE IN TETANUS*

E. ZOLLICOFFER BROWNE, M. D.†
AND
HARRY A. STONE, M. D.†
NEW ORLEANS

CASE REPORT

T. H. H., a white male, was first seen in the Emergency Room of the Southern Baptist Hospital in New Orleans on March 10, 1947 at 6 a. m., complaining of stiffness of the lower jaw; stiffness and soreness of the muscles of the neck, chest, back and abdomen; pain and soreness of right thumb. A history, obtained from his wife, revealed that he had stuck a splinter under cuticle of right thumb two weeks previously, while fishing. He removed what he thought was all of the splinter at that time, but received no medical attention for the injury. He had never been actively or passively immunized against tetanus. On March 8, 1947, stiffness in jaw muscles and difficulty in opening mouth first became apparent. The symptoms progressively grew worse and on the evening before admission marked stiffness and soreness in muscles of jaw, neck, chest and back ensued, with inability to open mouth more than a quarter of an inch. Some difficulty in swallowing was also noted.

Physical examination revealed a well developed, fairly well nourished white male, weighing about 150 pounds, appearing acutely ill, excited and apprehensive. There was marked rigidity of the muscles of the jaws and neck. Plainly in evidence was a typical "risus sardonicus." The abdomen was tense and rigid, but not tender on pressure. Opisthotonos was also noted. The distal phalanx of the right thumb was reddened and swollen on its dorsal aspect and showed a small area of suppuration under mid-portion of cuticle. The temperature was 98.2°, pulse 95, respiration 26, blood pressure 142/80.

The *history* of a splinter stuck in the thumb—with no after care—the general physical findings and the symptoms presented made it fairly easy to rule out other pathologic conditions which must be considered—such as, meningitis, infection at root of third molar tooth, peritonsillar abscess, strychnine poisoning and tetany. So a diagnosis of tetanus was made and the patient was admitted to the hospital.

Immediately after his admission he was given skin and conjunctival tests for sensitivity to horse serum. These being negative, 100,000 units of antitetanus serum was given intravenously and 18,000 units into tissues of right thumb. Amytal gr. 11 was injected intravenously at this time. At 9 o'clock a. m., he was taken to operating room where a wood splinter 1.5 c.m. long was removed and the adjacent area of thumb widely opened and drained. Intravenous sodium pentothal, supplemented with nitrous oxide, was used for anesthesia. Three c.c. Intocostrin* was given intravenously during the operation with marked relaxing effect on the generalized muscle spasm. It was decided then to continue the use of this drug and 1.5 c.c. was ordered to be given every four hours, either intravenously or intramuscularly, as best tolerated. This was done night and day until March 18, 1947 (eight days), when it was reduced to three times

*Presented at Staff Meeting of Southern Baptist Hospital on April 22, 1947.

†From the Staff of Southern Baptist Hospital, New Orleans, Louisiana.

*The Squibb preparation of purified Chondrodendron tomentosum extract in aqueous diluent.

daily and continued thus until March 22. It proved to be very helpful and markedly reduced the use of sedatives and hypnotics. On one occasion an intravenous injection relaxed the patient so much that breathing was entirely by diaphragm and speech was extremely slurred. Prostigmin, as an antidote, and oxygen were kept immediately available, if respiration should become too markedly reduced. However, neither was used.

An additional 100,000 units A. T. S. intravenously was given at 3 p. m. of the day of admission and 50,000 units thereafter daily, intravenously, until March 17, when it was discontinued because of serum reaction. One intrathecal injection of 20,000 units was given on March 13. Penicillin was started the afternoon of admission with a dosage of 40,000 units intramuscularly every three hours and was continued until March 20, a total of 3,200,000 units. Benadryl, 50 mgm. t. i. d. was given from March 17 to 20.

Laboratory Findings: Urine was found to be negative, except for a faint trace of albumin and an occasional white blood cell and red blood cell. Blood picture showed 4,200,000 red blood cells; hemoglobin 12 gm. (83 per cent); total leukocytes 10,650; neutrophiles 87 per cent, lymphocytes 7 per cent, eosinophiles 3 per cent, monocytes 3 per cent. Wassermann was negative. Blood chemistry: Total N. P. N., 39.3 mgm. per 100 c.c.; urea nitrogen, 14.7 mgm.; creatinine, 1.5 mgm.; uric acid, 2.0 mgm.; dextrose, 100 mgm. Spinal fluid: Negative. Sedimentation index, 14 mm. in 60 minutes.

Course in Hospital: The temperature remained normal until March 12 when it rose to 102° F. and remained elevated until March 16, when it returned to normal. A portable x-ray of the chest taken on March 15 was negative for pulmonary congestion.

The patient was delirious during the first four days and made several attempts to get out of bed. Once he fell but sustained no apparent injury except a small abrasion of the scalp. It was later discovered that he was attempting to jump from window as he thought he was going to die. He was given occasional doses of a barbiturate for sedation and narcotics as needed for pain. However, not much of these drugs were required, as above stated. A liquid diet was given until March 18 on account of inability to chew. The dressing on thumb was changed daily.

The patient gradually improved and on March 19 a diet was ordered as desired. He was allowed up in wheel chair on March 22. On this day he walked, but with much difficulty due to stiffness of the back. The ability to walk rapidly improved and he was discharged on March 24, 1947. At this time the infected thumb was almost healed.

CLINICAL DISCUSSION

Not overlooking the great value of tetanus antitoxin and barbiturates (and the questioned value of penicillin) in contributing to this recovery, I wish to stress the valiant role played by Intocostrin, as I believe the patient would have died of exhaustion—due to the widespread massive spasm of his skeletal muscles, had we not had the relaxing effect secured by this drug. "The typical curare action" consists essentially of an interruption of nervous impulses to skeletal muscle at the myoneural junction. When Intocostrin is introduced intravenously it rapidly produces a paralysis involving the skeletal muscles, the diaphragm and intercostals being last to be affected. The drug is excreted so rapidly that the duration of maximum effect is transient. This relaxing effect was a source of great relief to this patient undergoing massive spastic contraction. *Care and constant supervision of a patient receiving continuous relaxation, at or near, the level of respiratory paralysis is most important*, as experimental work indicates that the resultant hemoconcentration which apparently arises from loss of fluid from the vascular system into the relaxed muscles, may induce a state of shock. Adequate care in the amount of dosage and use of other measures to combat shock will materially lessen this danger, which after all, is certainly a lesser danger than would be faced if we did not have this drug in our armamentarium.

NEW ORLEANS
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Established 1844

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THE STATE SOCIETY MEETING

The 68th Annual Meeting of the Louisiana State Medical Society will take place in Monroe on April 12-14. An attractive program has been prepared. The major portion of the first day, April 12, will be consumed by the two sessions of the House of Delegates. The business affairs of the Society and its relation to government interference require your earnest consideration. Important matters are to be reviewed at the several sessions.

It will be noted, by studying the tentative program in this issue, that the committee has followed the recent trend of grouping related subjects in symposia on April 13, the second day of the meeting. At the same time the needs of specialty groups have been met by arranging five sectional meetings, morning and afternoon, on Wednesday, the last day.

Of special interest will be the cancer symposium; hormone, tissue culture, hereditary and surgical features are being discussed in six concise papers. The symposium on medical diseases of the kidney will prove very interesting to the internist and to general practitioners.

The Society is fortunate in having ten guest speakers. They are:

Dr. Morris Fishbein, Chicago
Dr. James Ernest Ayre, Montreal
Dr. Ira T. Nathanson, Boston
Dr. Harry S. N. Greene, New Haven
Dr. J. E. Faber, Rochester, Minn.
Dr. F. R. Lock, Winston-Salem
Dr. Wm. F. Guerriero, Dallas
Dr. Herbert Mantz, Kansas City, Mo.
Dr. W. Ambrose McGee, Richmond
Dr. George B. Eusterman, Rochester, Minn.

The program committee is to be congratulated on having arranged so inviting a program and it is anticipated that the members who attend will have a lively interest in the proceedings.

—o—

STATE PROVISION FOR THE NATION'S HEALTH

The President of the United States, in his message to Congress on January 7, asked for " a national system of payment for medical care based on well tried insurance principles". In this section of the message and in the discussion of education the word "compulsory" was not noted. There was a request for an executive department or cabinet post for "health education and security". It may be expected, therefore, that other bills of the type typified by the Wagner-Murray-Dingell Bills will be forthcoming with the compulsory

feature submerged and the desirable change of a cabinet post for health will be offered. Efforts in the Congress to establish "state medicine" in some of its forms have been fought by the medical profession. After successive defeats the advocates of these bureaucratic experiments have changed the form in which the plan was presented. We anticipated, accordingly, a bill with some desirable or questionable features and many objectionable ones. It is necessary for the physicians to continue to be on the alert; to examine the proposals that are presented to Congress in any guise. We should acquaint ourselves and our patients with what others would like to put on them in the form of taxation, bureaucratic control, and professional embarrassment.

In 1917 the constitutional amendment allowing income taxes was quietly passed by the various theorists and social planners. The laws enacted under this amendment have grown. The regulations promulgated in accordance with such authority now constitute volumes. As a result the affairs of income tax have become a concern of every individual under the flag. It affects every wage earner — bookkeeper, professional man, business man—everyone with an income. Every business policy or financial move has to be examined in the light of the income tax law. It will probably be found ultimately that the income tax will produce, in time, the panics in finance that our Federal Reserve Banking policies were designed to prevent. If the legislators who ratified the amendment 31 years ago had any idea of the extent of the effect of this law, the vast majority would have been afraid to approve it.

By the same token "health legislation", on a national scale, with or without the word compulsory, bears the same threat. As practitioners of medicine we have our freedom now. We also have the power to oppose being regimented. The statement which came down from one of the founders of our Country; "The power to tax is the power to destroy", was never more true than now.

TENTATIVE PROGRAM

1948 ANNUAL MEETING—FRANCES HOTEL—MONROE

MONDAY, APRIL 12

ROOF

9:00 A. M.	House of Delegates
Luncheon	House of Delegates
2:00 P. M.	House of Delegates
8:00 P. M.	General Public Meeting 1. *Morris Fishbein, M. D., Chicago 2. Cytologic Diagnosis of Cancer—James Ernest Ayre, M. D., Montreal *Subject to be announced

TUESDAY, APRIL 13

ROOF

9:00 A. M.	**Symposium on Cancer:** Ambrose Storck, M. D., New Orleans 1. The Influence of Sex Hormones and Castration on Advanced Cancer of the Breast and Prostate—Ira T. Nathanson, M. D., Boston, Mass. 2. The Incidence and Management of Lymph Node Involvement in Cancer—Ira T. Nathanson, M. D., Boston, Mass. 3. Clinical Application of In Vivo Tissue Culture—Harry S. N. Greene, M. D., New Haven, Conn. 4. Recent Advances in the Treatment of Carcinoma of the Cervix and Fundus—E. Perry Thomas, M. D., New Orleans 5. Genetics and Cancer—Walter J. Burdette, M. D., New Orleans 6. Carcinoma of the Colon and Rectum—S. A. Romano, M. D., L. H. Kuker, M. D., and C. C. Craighead, M. D., New Orleans
Luncheon	General Membership
2:00 P. M.	*__Symposium—Medical Diseases of the Kidney:__ Samuel B. Nadler, M. D., New Orleans *Subjects to be announced
8:00 P. M.	President's Reception

WEDNESDAY, APRIL 14

9:00 A. M.	
ROOF	House of Delegates
ROOM A	**Obstetrics:** R. B. Wallace, M. D., Alexandria 1. Clinical Experience with the Rh Factor in Obstetrics—E. L. King, M. D., and John A. King, M. D., New Orleans 2. Management of Premature Labor—C. J. Lund, M. D., New Orleans 3. Experiences with Anti-Coagulants in Postpartum Patients—J. E. Faber, M. D., Rochester, Minn. 4. Maternal Mortality in the South—F. R. Lock, M. D., Winston-Salem, N. C. **Gynecology:** Conrad G. Collins, M. D., New Orleans 1. Some Clinical Considerations on the Sterility Problem from the Viewpoint of the Gynecologist—B. B. Weinstein, M. D., New Orleans Discussion—C. R. Mays, M. D., Shreveport 2. Retrodisplacements of the Uterus—Peter Graffagnino, M. D., New Orleans Discussion—Howard P. Hewitt, M. D., Lafayette 3. Menopausal Bleeding—C. H. Tyrone, M. D., New Orleans Discussion—R. E. C. Miller, M. D., Alexandria 4. Gyn-Like Complaints—Wm. F. Guerriero, M. D., Dallas, Texas Discussion—Jack R. Jones, M. D., Baton Rouge
ROOM B	**Medicine:** M. W. Hunter, M. D., Monroe 1. Drugs of the Present and Future—P. M. Tiller, Jr., M. D., New Orleans 2. Gastroscopy—Carl Rabin, M. D., New Orleans Discussion—Felix J. Willey, M. D., New Orleans 3. Unusual Manifestations of Coronary Heart Disease—T. H. DeLaureal, M. D., Lake Charles Discussion—Manuel Gardberg, M. D., New Orleans 4. Modern Advances in Diabetes Mellitus—Frank W. Pickell, Jr., Baton Rouge 5. Treatment of Acute Brucellosis, T. B. Tooke, Jr., M. D., Shreveport **Orthopedics:** Geo. C. Battalora, M. D., New Orleans 1. Specific Treatment of the Fractured Ankle—Irving Redler, M. D., New Orleans
ROOM D	**Radiology:** John M. Miles, M. D., Lafayette 1. *D. D. Moore, Monroe **Neuropsychiatry:** Walter J. Otis, M. D., New Orleans 1. Psychosomatic Problems in Adolescents—Herbert E. Harms, M. D., New Orleans 2. Psychiatric Emergencies—Max Johnson, M. D., New Orleans **Public Health:** Wm. M. Johnson, M. D., Leesville 1. Diagnosis of Tuberculosis—Herbert Mantz, M. D., Kansas City, Mo. 2. Ignorance is Not Bliss—M. P. Martin, M. D., New Orleans *Subject to be announced

(Continued on Next Page)

(Continued from preceding page)

ROOM 210

Bacteriology and Pathology: Edwin H. Lawson, M. D., New Orleans
1. Human Equine Encephalomyelitis (Eastern Type) in Louisiana—George H. Hauser, M. D., New Orleans
2. Encephalomyelitis (Eastern Type) Occurring in Horses and Mules in Louisiana—E. P. Flower, D. V. S., Baton Rouge
3. Causes and Prevention of Transfusion Reactions—J. W. Davenport, M. D., New Orleans
4. Pathology of Transfusion Reactions—S. H. Colvin, M. D., New Orleans

Eye: Wm. B. Clark, M. D., New Orleans
1. The Role of Early Retrobulbar Neuritis in Management of Senile Cataracts—Shelley R. Gaines, M. D., New Orleans

Luncheons

Obs. & Gynecology	Tuberculosis-Histoplasmosis in La.—Herbert Mantz, M. D., Kansas City, Mo.
Medicine	Pediatrics—no luncheon*
Orthopedics—no luncheon	Allergy—no luncheon
Radiology	Dermatology—no luncheon
Neuropsychiatry—no luncheon	Urology
Public Health	Surgery—no luncheon
Bacteriology and Pathology	Gastro-enterology
Eye—no luncheon	*Dinner

2:00 P. M.

ROOM A

La. Tuberculosis Assn.: Sydney Jacobs, M. D., New Orleans
1. Some Data Pertinent to the Diagnosis and Prognosis of Pulmonary Tuberculosis—Philip B. Johnson, M. D., and Louis A. Monte, M. D., New Orleans
2. X-ray Diagnosis of Pulmonary Tuberculosis—J. E. Blum, III, M. D., Greenwell Springs
3. Collapse Therapy in the Treatment of Tuberculosis—Dewey L. Anderson, M. D., Monroe
4. Recent Trends in the Surgery of Pulmonary Tuberculosis—Louis F. Knoepp, M. D., Shreveport
5. Streptomycin in the Negro with Tuberculosis—Nathan Goldstein, M. D., New Orleans
6. X-ray Conference—Maurice Campagna, M. D., New Orleans

ROOM B

Pediatrics: R. V. Platou, M. D., New Orleans
1. Clinical Features of a Summer Epidemic Disease (Three Day Fever)—Clarence H. Webb, M. D., and S. George Wolfe, M. D., Shreveport
2. Epidemiological Studies on Three Day Fever—Verre Simpson, M. D., Shreveport
3. Postgraduate Education in Pediatrics for General Practitioners—Sidney S. Chipman, M. D., New Orleans
4. Kerosene Poisoning—N. Bologna, M. D., and N. Woody, M. D., New Orleans
5. Advantages of Early Recognition and Treatment of Allergic Disorders of Infancy and Childhood—W. Ambrose McGee, M. D., Richmond, Va.
6. Diagnosis at a Glance—Conway S. Magee, M. D., Lake Charles

ROOM D

La. State Allergy Society: B. G. Efron, M. D., New Orleans

CASE REPORTS:
1. Contact Dermatitis—Henry D. Ogden, M. D., New Orleans
   Discussion—R. E. Selser, M. D., Baton Rouge
2. Treatment of Asthma with Isuprel—H. Whitney Boggs, M. D., Shreveport
   Discussion—Dewey L. Anderson, M. D., Monroe
3. Provocative Test in Hypersensitivity—Stanley Cohen, M. D., New Orleans
   Discussion—B. G. Efron, M. D., New Orleans
4. Possible Allergy in Dermatomyositis—W. H. Browning, M. D., Shreveport
   Discussion—J. Dudley Youman, M. D., Shreveport
5. Purpura Due to Allergy—B. G. Efron, M. D., New Orleans
   Discussion—Vincent J. Derbes, M. D., New Orleans

ROOM 210

Dermatology: Medd Henington, M. D., New Orleans
1. Eruptions of the Hands and Feet and Their Treatment—Barrett Kennedy, M. D., New Orleans
2. The Treatment of Certain Dermatoses with Oral Bismuth—J. K. Howles, M. D., New Orleans

Urology: DeWitt T. Milam, M. D., Monroe
1. Modern Treatment of Urinary Tract Infections—Hugh T. Beacham, M. D., New Orleans
2. Retropubic Prostatectomy (moving picture)—R. K. Womack, M. D., Shreveport.

ROOF

Surgery: J. D. Rives, M. D., New Orleans
1. Decortication of the Lung—Walter W. McCook, Jr., M. D., Shreveport
2. Combined Abdomino-Thoracic Injuries—Donald B. Williams, M. D., Lafayette
3. Vascular Injuries—Paul D. Abramson, M. D., Shreveport
4. The Pre and Postoperative Management of the Substandard Surgical Risk—Champ Lyons, M. D., New Orleans

Gastro-enterology: T. B. Tooke, Jr., Shreveport
1. Penicillin in Treatment of Peptic Ulcer—R. W. Young, M. D., Baton Rouge
2. Newer Aspects of the Management of the Peptic Ulcer Patient—George B. Eusterman, M. D., Rochester, Minn.
3. Round Table Discussion—Vagotomy: Its Surgical and Medical Aspects—George B. Eusterman, M. D., Rochester, Minn.; Gordon McHardy, M. D., New Orleans; Howard R. Mahorner, M. D., New Orleans; R. M. Penick, Jr., New Orleans

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ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

INTERIM MEETING
A. M. A. HOUSE OF DELEGATES

Members of Executive Committee
Louisiana State Medical Society
1430 Tulane Avenue
New Orleans 13

Gentlemen:

Following is a report of the interim meeting of the American Medical Association House of Delegates held on Monday and Tuesday, January 5 and 6, 1948 in Cleveland, Ohio. Dr. Graves and I, Delegates to the meeting, thought it would be interesting to the members of our State Society to know just what has taken place at this meeting and hence this report.

The meeting was called to order shortly after ten A. M. by the Speaker of the House, Dr. R. W. Fouts, of Omaha, Nebraska. The Chairman of the Reference Committee on Credentials reported 138 accredited delegates. The Speaker then announced the appointment of his committees and Dr. Graves was appointed to the Elections Committee and I was appointed to the Committee on Sections and Section Work.

The names of three general practitioners were then submitted for the General Practitioner's Award. The final vote showed that Dr. A. C. Sudan, of Colorado, received a majority vote on the first ballot and he was designated the winner of the medal.

Remarks of the President and President-elect and report of officers and committees was the next order of business. Following this adjournment took place until two-thirty in the afternoon, when reports were received.

The first report was a very lengthy one by the Committee to Expedite Work of the House of Delegates. Since the Annual Meeting covers four full days and the Interim Meeting only two days a complete agenda for both meetings was presented and adopted. There is no need to burden you with the order of business of these two different sessions as I am sure they will appear in the Journal of the A.M.A.

A uniform method of electing delegates was decided upon. This new system is the one used by the Louisiana State Medical Society so there will be no change in our present method of election of delegates.

Recommendation was adopted that it be a standing rule that the Speaker of the House appoint reference committees two months in advance of a session and that the list of appointments be published one month in advance of the session. This is in contradiction to what is being done at the present when the Speaker of the House announces the committees as the first order of business.

There was a rather controversial discussion of just what an executive session of the

House means and this was clarified to the satisfaction of all of the delegates.

The Committee on the Constitution and By-Laws has almost finished its extensive work and the committee feels sure that it will be able to submit its final draft at the June meeting in Chicago.

There was some discussion about the time of the Interim meeting this year since it was held when thousands of college and school students were on their way back from the Christmas holidays. It was decided that the usual time for the Interim Meeting would be in the month of December unless accommodations can not be obtained; under such conditions the decision will be left to the Board of Trustees.

It was brought out that the A.M.A. worked with a deficit of over $100,000.00 during the past year and a recommendation was made and passed that the dues for 1948 should be increased to $12.00. After this year the Board of Trustees will have the authority to raise the dues to any amount not exceeding $12.00.

A Committee from the A.M.A., the American Hospital Association and the American Nurses Association, consisting of fifteen members, was recommended; this committee to be known as "a coordinating committee for the study of nursing problems".

Approval was given for the formation of a Committee on Multiple Sclerosis Program of Education.

A committee was appointed to study the formation of regulations governing rotating internships in hospitals before a doctor is permitted specialty training. This committee is also to formulate plans to staff hospitals with interns by limiting the number of interns to the bed capacity of the hospital. This will be a committee of five, two of whom are to be general practitioners, and the committee is to report at the Annual Meeting in June. They are also to stress the formation of a Residency of general practice in hospitals.

A classification of medical students in some form of membership in the A.M.A. is now under consideration.

Dr. Bortz complimented the work of the Woman's Auxiliary and exhorted the delegates to organize such auxiliaries in states where none are present.

Case findings with x-ray have produced such great results in finding of tuberculosis that the A.M.A. will endeavor to further measures to make as widespread as possible the dissemination of this information and it was agreed that complete physical examination, including x-rays of the chest would be required of all immigrants before they are admitted to this country.

A resolution limiting the term of delegates was *not* approved.

Another resolution asking for a better geographical distribution of the Board of Trustees failed to pass.

The so-called exploitation of the x-ray and pathological departments by hospitals was referred to a new committee that is to be appointed to study this problem and to report at the June meeting.

The brochure as presented by the Committee on Rural Medical Service was distributed and the committee was congratulated for the excellent work it has accomplished. We were pleased to see the excellent report from the Chairman of our State Committee in this brochure.

The reference committee to study the Blood Bank of the Red Cross approved again, in principle, the establishment of blood banks by the American Red Cross provided that the American Red Cross accept the following principle: To insure safety to recipients, the responsibility for technical details must rest on properly trained personnel under the control of local or state medical societies. The committee further recommends that the American Red Cross be asked to accept a permanent committee from the A.M.A. to coordinate the medical work of the Red Cross.

It was reported that the News Letter is now being sent to approximately 3500 practicing physicians in the United States and that any doctor who desires to receive this can apply to the A.M.A. to be placed on the mailing list.

It was brought out that any prepayment medical plan, whether profit or non-profit, if it is acceptable to the county or state medical society, may apply for recognition in the Associated Medical Care Plans, however they must meet certain requirements before being accepted. No doubt you have seen in the newspapers of Sunday, January 11, that General Hawley, former director of the medical services of the Veterans Administration, will be the coordinator or director of a combined committee of the Blue Cross Commission and Associated Medical Care Plans.

The interim session adjourned on Tuesday afternoon at four-thirty.

On Monday evening at seven o'clock a joint dinner of the delegates was held with the members of the Council on Industrial Health, sponsored by the Cleveland Chamber of Commerce and the Cleveland Academy of Medicine. This was a very interesting meeting with some excellent motion pictures of atom bomb destruction at Bikini. Also a patient was brought over from New York and demonstrated as an example of what can be accomplished by rehabilitation training. This was a young man who had suffered from poliomyelitis and both arms and both legs were involved.

Dr. Graves received the assurance of Dr. Morris Fishbein that he will attend and address the Annual Meeting of the Louisiana State Medical Society in Monroe.

If there is any further information any member of the Executive Committee desires I am sure Dr. Graves or I will be glad to furnish whatever we can.

Respectfully submitted,

VAL H. FUCHS, M. D.,
Delegate.

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LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

PUBLIC RELATIONS PROGRAM ANNOUNCED BY COUNCIL

The public relations program for the year 1948 was announced recently by Dr. A. V. Friedrichs, Chairman of the Council on Medical Service and Public Relations and will be mailed to all members of the State Society.

The purpose of this program shall be to further a better understanding of problems common both to the laity and the profession, to disseminate information which is of general interest and value to keep both the public and the medical profession informed of significant progress in the field of public relations.

The program is to be promulgated under the leadership of the Council on Medical Service and Public Relations in cooperation with the Executive Committee and the House of Delegates of the Louisiana State Medical Society, and is to serve as a guide-post to component parish medical societies and their respective committees.

The public relations program is composed of the following projects:

1. Professional Relations between Physicians.
2. Professional Relations with Allied Professions and Auxiliary Groups.
3. General Public Relations.
4. Promotion of Voluntary Health Insurance.
5. Relations with Civic Agencies and Societies.
6. Relations with Government Agencies.
7. Relations with Civic Clubs.
8. Relations with Molders of Public Opinion.
9. Patient-Physician Relations.
10. Public Relations in Rural Health.

11. Assist in Establishing Health Councils.
12. Miscellaneous.

The Council has an overall program proposed which will take quite some time to develop in its entirety. There are a number of important phases associated with the Council's program, especially under the heading of "general public relations", and it is proposed to establish ultimately an active News Bureau and through this medium keep the general public properly informed of news pertaining to the medical profession.

Another important phase of the program is the establishment of Health Radio programs throughout the State of Louisiana on as many radio stations as it is possible to secure time as a public service feature. One radio program has already been started and within a short time a number of other programs will be announced. It is also proposed that a Speakers' Bureau be established both on a statewide basis and on a parish or community basis. Through the medium of this Bureau, speakers will be made available to civic clubs, women's clubs, political rallies, government hearings, and on all occasions when a prominent speaker is necessary to discuss such subjects as voluntary health insurance, compulsory health insurance, health, physical and safety education, public health, the operations of a medical society, socialized medicine, and numerous other subjects of public interest.

The cooperation of every component medical society will be needed to successfully present this public relations program. The Woman's Auxiliary to the various parish medical societies can be of great value to the Council in assisting it in fulfilling its objective.

A copy has been mailed to every member of the Louisiana State Medical Society and we ask that you review same and keep it in your files for future use. You will see that it contains many phases in which each member of the medical profession can actively participate. Your wholehearted cooperation in its presentation and fulfillment will be your answer to offset the government's cry for socialization of medicine.

PUBLIC RELATIONS COUNCIL STARTS FIRST BROADCAST

The first of a series of broadcasts, presented by the Council on Medical Service and Public Relations of the Louisiana State Medical Society in cooperation with the Ouachita Parish Medical Society and its Woman's Auxiliary, was presented on Wednesday, January 14 over Radio Station KNOE in Monroe. The series consists of 13 weekly broadcasts of 15 minutes each and is entitled "Before the Doctor Comes".

The series is a practical, reassuring group of interviews in which the mother asks the doctor what to do about her everyday health problems. The series tells what to do "Before the Doctor Comes" in case the patient is suffering from sniffles, sore throat and coughs, fever, rash, headache, earache, or in cases suffering from bad bumps or other accidents. Radio Station KNOE in Monroe has donated this time as a public service feature to the Council on Medical Service and Public Relations.

The broadcasts will be from transcriptions prepared by the American Medical Association. Material is from the library and publications of the A.M.A. Numerous eminent physicians, both in medical practice and public health work, have been brought before the microphone to be interviewed. All scripts are professionally prepared by experienced radio writers and the voice of the interviewer is that of Harriet Hester, formerly of the staff of WLS of Chicago, well-known NBC interviewer. Harriet Hester and William J. Murphy, veteran writer of medical scripts, have written the continuity. In the musical portion of the program, Elwyn Owen is at the organ.

The preparation of the series is under the general direction of Dr. W. W. Bauer, Director of Bureau of Health Education of the American Medical Association, who appears on the program and his associate in the bureau, Dr. William W. Bolton. The broadcast was made possible through the wholehearted cooperation of Mr. R. W. Dumm, General Manager of KNOE.

Members of the Public Relations Committee of the Woman's Auxiliary to the Ouachita Parish Medical Society assisted in the arrangements and presentation of the broadcast in that area. Members of the committee are Mrs. H. B. Collins, Chairman; Mrs. C. B. Flinn; Mrs. C. P. Gray, Jr.; Mrs. Hayden Cutler; and Mrs. J. E. McConnell.

HEALTH BROADCASTS NOW AVAILABLE TO PARISH SOCIETIES

Series of transcribed health broadcasts are now available and may be presented by the parish medical societies in cooperation with the Council on Medical Service and Public Relations of the Louisiana State Medical Society, Frank Lais, Jr., Executive Director of the Council announced recently.

The programs are of a 15-minute duration to be presented weekly and will be furnished to any radio station selected by the parish medical society, at no cost to the station or the society. All organizations interested in presenting a series of health broadcasts in their community should contact the office of the Council, Room 103, 1430 Tulane Avenue, New Orleans, Louisiana.

WHAT OTHER STATES ARE DOING IN REGARD TO PUBLIC RELATIONS

After a meeting of the Virginia Medical Public Relations Conference, held in Richmond, Virginia,

on December 20, a report was prepared by Frank Lais, Jr., Executive Director of the Council on Medical Service and Public Relations.

We thought it would be interesting to know what some of the other states are doing in public relations and also some of the comments made by persons closely associated with the medical profession.

Dr. Walter B. Martin of Norfolk, Virginia, member of the Council on Medical Service of the A.M.A., spoke on benefits of medical care under a voluntary system. He paid a particular compliment to the Southern Regional Conference held in New Orleans and expressed the desire for semi-annual conferences such as the one held and also commented on the value of the conferences held in Atlanta and Philadelphia. He advised the group that it was through this medium that the A.M.A. is bringing information to the individual state societies. He stated that the A.M.A. District Councils have been organized and that the A.M.A. will use the Councilors as contact men. He stated that the A.M.A. cannot formulate an overall program of medical care that will satisfy all sections of the country—all plans should be formulated on a district or local basis and that public opinion should be developed in the local areas.

He stated that the A.M.A. can only be used to formulate policies and evaluate certain principles, and that the implementation of any program must go back to the individual state societies. He strongly recommended the formation and organization of state, parish and local health councils—health councils should include lay individuals and representative citizens. The council should be composed of 15 or 20 individuals including two or three doctors. He stated that doctors should not dominate the council or try to control it but should take leadership in the operation. He stated that the council should be an influence on the type of medical care that is available, and should not be organized on the basis of personal gain for individuals. They should be impressed as to the advantages of good medical care and also why certain practices such as that of chiropractors and naturopaths are not acceptable.

He cautioned members about sidetracking such programs as the V.A. program and the Coalminers Medical Care. He stated that the coalminers program may include 16 to 20 million people, and 50 to 60 million persons, including veterans and their dependents, will ultimately be covered by the V.A. program. He stated that if such programs are carried out on an individual basis, it would eliminate a large quantity of medical care from the community and he urged all doctors to cooperate with these services to keep them on a local basis. If this is not done on a community basis, large groups will be organized on a national basis and little will be left on an individual basis.

Dr. J. M. Emmett, Chairman of the Public Relations Committee of the Medical Society of Virginia, stated if doctors do not assume the responsibility of the distribution of medical care, then the Federal Government will take over the provision of this care. Doctors should not however dominate the local health councils and should use lay individuals to assist them in the local health councils. The interest of adequate medical care is being sponsored by too small a group of individual doctors and he urged more doctors to become interested in the promotion of adequate medical care. Adequate medical care must be presented by large groups of doctors and a small group of standard-bearers should not be forced to carry the load.

He stated that an attempt to tell the people that the practice of medicine is perfect, is wrong, because it is not perfect. It is doubtful that the public believes that medicine as it is today is on an adequate basis. The system is as far advanced as a group can go individually. Surely, there is no better way than to keep medicine as a private practice but the secret is to get the people who believe as do the doctors to associate with them.

Dr. H. B. Mulholland, a member of the Public Relations Committee and Assistant Dean of the University of Virginia Medical School, stated that the people are now interested in adequate medical care and that much of the need for medical care has come out of Washington rather than from the doctors themselves. Doctors have been more interested in the delivery of medical care than in seeing that all have adequate medical care.

Doctors must show the people—even though the doctors provide adequate facilities, the people must be educated to use these facilities and shown how to use them when they are available. He suggested that this be started in the schools and that doctors must be leaders in their community in the organization of health councils. The doctor must discuss his problems with other leaders and he should be particularly informed on the availability of prepayment medical care insurance because most people are interested in acquiring health insurance.

Dr. L. J. Roper, a member of the Public Relations Committee and Commissioner of Health for the State of Virginia, stated that the relationship of public health services and the doctors depends upon the cooperation of both groups. The relationship between the two groups is broadening considerably throughout the nation. Both are working harmoniously in Virginia. He stated that his public health department has implemented a program for cancer and for other services far ahead of the old public health program. He stated that there was a time when the relationship between the two groups was not too good but now the differences have been adjusted.

The public health program of Virginia utilizes the services of physicians and physicians are al-

ways willing to help. He said the public health service now uses the services of all physicians in the examination of school children.

Health officers in Virginia are the friends of the doctors and it is their desire to cooperate in every way. The public health doctor in Virginia is considered as a "wholesaler" because he deals with the masses, and the individual doctor is the "retailer" of medical services because he deals with the individual.

Dr. William Shands Meacham, Director of the Virginia Council on Health and Medical Care, spoke on the organization of health councils on a state, county, and community basis in Virginia. The health council in Virginia is organized on an incorporated basis, separate from any particular organization. All of the health councils are supported by voluntary contributions from all cooperating government agencies, the medical societies, and other interested individuals.

Dr. W. R. Pretlow, President of the Virginia Medical Service Association (the Virginia prepayment medical care plan), advised the physicians present that it is up to the doctors in their individual state to do something for the people who are in need of medical care or the government is going to do it. He does not believe that talking to Congressmen, talking to your nextdoor neighbor, articles in the newspapers about the fallacies of socialized medicine are sufficient. These will offer only temporary relief and the medical profession will still be in a state of emergency.

The only assurance against socialized medicine is for the doctors to get behind their voluntary prepayment insurance plans and actively promote them so that people will be protected, and then, and only then, will there be an answer to the government's demand.

People will feel the need for medical care plans during the next depression and the doctors should get behind the plans to enroll everyone. He earnestly recommends the inclusion of promotional literature in the monthly bills of each physician.

The most enlightening and constructive paper of the day was delivered by Dr. John T. Hundley, a member of the District Council—Lynchburg Academy of Medicine. Dr. Hundley conducted an individual survey to determine the attitude of a selected group of individuals toward the medical profession. The survey included newspaper editors, union leaders, bankers, lawyers, persons in every walk of life, rich and poor, persons who are confined to some of their charity institutions. The survey asked that these individuals list any grievance of which they have knowledge pertaining to the medical profession. His survey was startling and members in attendance were wide-eyed as he read some of the comments from his survey.

The survey prepared by Dr. Hundley is to be mimeographed and possibly reproduced in the A.M.A. Journal.

Dr. Guy Fisher, President of the Medical Society of Virginia, in closing the meeting, stated that the humanitarian spirit of medicine is lacking and that is one reason why the laity is doubting the medical profession.

ORGANIZATION OF HEALTH COUNCIL

Citizens of Lake Providence recently met in the courthouse for the purpose of organizing a permanent health council. The meeting was called in cooperation with the East Carroll Parish Farm Bureau and the Council on Medical Service and Public Relations of the Louisiana State Medical Society. About two hundred persons attended the meeting and unanimously endorsed the organization of a permanent health council in East Carroll Parish. Dr. Forrest M. Terral of Lake Providence was elected permanent chairman of the East Carroll Parish Health Council.

Dr. John Snelling of Monroe represented the Council on Medical Service and Public Relations and talked on the advantages to be obtained through the organization and establishment of a health council. Also attending the meeting were Frank Lais, Jr., Executive Director of the Council on Medical Service and Public Relations and Mr. P. A. Colvin of Monroe, who explained the advantages of voluntary health insurance. Also appearing on the program were Mrs. T. R. Tomlinson, Chairman of the Louisiana Rural Health Council, and Miss Mary Mims, State Extension Sociologist.

A representative from the department of Institutions also appeared before the council and interested the group in the construction of a hospital in the Lake Providence area.

NEW OFFICERS OF COMPONENT SOCIETIES

The following officers have been elected by their respective parish societies to serve for 1948.

Avoyelles Parish Medical Society—
President—Dr. James Knoll, Bunkie
Vice-Pres.—Dr. Philip P. Giuffre, Cottonport
Sec.-Treas.—Dr. S. R. Abramson, Marksville
Delegate—Dr. Kirby A. Roy, Mansura

Beauregard Parish Medical Society—
President—Dr. John D. Frazar, DeRidder
Vice-Pres.—Dr. Luke M. Marcello, DeRidder
Sec.-Treas.—Dr. Sam T. Roberts, DeRidder
Delegate—Dr. John D. Frazar, DeRidder
Alternate—Dr. Luke M. Marcello, DeRidder

Claiborne Parish Medical Society—
President—Dr. S. A. Tatum, Homer
Vice-Pres.—Dr. J. E. Batchelor, Haynesville
Sec.-Treas.—Dr. Martin L. Forcht, Haynesville
Delegate—Dr. Thomas M. Deas, Homer
Alternate—Dr. J. W. Featherston, Homer

DeSoto Parish Medical Society—
President—Dr. W. B. Hewitt, Mansfield

Vice-Pres.—Dr. R. P. Thaxton, Mansfield
Sec.-Treas.—Dr. R. A. Tharp, Mansfield
Delegate—Dr. R. A. Tharp, Mansfield

Franklin Parish Medical Society—
President—Dr. W. L. Strahan, Winnsboro
Vice-Pres.—Dr. John N. Bostick, Gilbert
Sec.-Treas.—Dr. A. J. Reynolds, Winnsboro
Delegate—Dr. H. T. Rogers, Winnsboro

Jackson-Lincoln-Union Parish Medical Society—
President—Dr. Carl F. Langford, Ruston
Vice-Pres.—Dr. T. D. Boaz, Jonesboro (Jackson)
Dr. W. P. Lambeth, Farmerville (Union)
Sec.-Treas.—Dr. John A. Thomas, Ruston
Delegate—Dr. T. A. Dekle, Jonesboro
Alternate—Dr. M. T. Green, Ruston

Jefferson-Davis Medical Society—
President—Dr. Morgan Smith, Jennings
Vice-Pres.—Dr. John G. McClure, Welsh
Sec.-Treas.—Dr. L. E. Shirley, Jennings
Delegate—Dr. John G. McClure, Welsh
Alternate—Dr. F. W. Harrell, Jennings

St. Landry Parish Medical Society—
President—Dr. F. O. Pavy, Leonville
Vice-Pres.—Dr. Charles W. Lewis, Eunice
Sec.-Treas.—Dr. C. L. Mengis, Opelousas
Delegate—Dr. F. Creighton Shute, Opelousas
Alternate—Dr. S. J. Rozas, Opelousas

St. Mary Parish Medical Society—
President—Dr. T. H. Gueymard, Morgan City
Vice-Pres.—Dr. C. R. Brownell, Morgan City
Sec.-Treas.—Dr. S. J. Russo, Morgan City

Vernon Parish Medical Society—
President—Dr. Joe E. Broyles, Leesville
Vice-Pres.—Dr. E. H. Byrd, Leesville
Sec.Treas.—Dr. William M. Johnson, Leesville
Delegate—Dr. William M. Johnson, Leesville
Alternate—Dr. M. W. Talbot, Leesville

RESIDENT NEEDED

Information has been received that there is need at this time for a part time resident at the Metairie Hospital in New Orleans. For further information contact the Secretary of the Hospital, Mr. J. Strauss, 310 Codifer Boulevard, New Orleans.

NEW ORLEANS ACADEMY OF INTERNAL MEDICINE

The newly formed New Orleans Academy of Internal Medicine held its first dinner meeting on Thursday, January 15, 1948.

Following a short business meeting and dinner, the guest speaker, Dr. Robert Nieset, delivered the address. His subject was "Some Relations of Modern Physics to Medical Research". Dr. Nieset is Director of Biophysics Research at Tulane University.

The officers of the new organization are Dr. Thomas Findley, President; Dr. Willard Wirth, Vice-President; Dr. Sam Nadler, Secretary-Treasurer, and Dr. Edgar Hull and Dr. Chaille Jamison, additional members of the Executive Committee.

The next meeting of the Academy will be some time in April, to be announced later.

APPOINTMENT OF COMMISSIONED OFFICERS IN THE MEDICAL CORPS AND DENTAL CORPS OF THE REGULAR NAVY

The statutory authority contained in Public Law 365—80th Congress, Title II (Army-Navy-Public Health Service Medical Officer Procurement Act of 1947) makes it possible now for civilian doctors to become commissioned officers in the regular Navy, provided they meet the professional and physical qualifications. This law is unique in that it does away with, for the first time, the age limitation of thirty-two years of age and permits doctors in civilian practice to enter the Navy and be commissioned with the rank up to and including Captain. The law considers all strata of the medical profession, internes, residents, reserves, former medical officers who have resigned, and present practicing physicians.

In order to make application a doctor must be a citizen of the United States, a graduate from a Class "A" medical school and have served at least one year's internship in an approved hospital. Candidates will then be judged on a number of qualifications such as being a member of a specialty board, his teaching connections, the number of years of professional or scientific practice, hospital or laboratory connections, a statement of military service, etc.

The allocation of rank to successful candidates will depend upon their academic age, professional standing, and experience in the medical field. Successful candidates will then be integrated in line with medical officers of the regular Navy and assigned running mates accordingly. This means that they will be eligible for promotion along with their fellow officers of equal rank.

This law offers a fine opportunity for civilian doctors to make a career in the regular Navy and to enjoy its professional advantages as well as its retirement benefits. Doctors interested in such a career should write to the Bureau of Naval Personnel, via the Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

NEW HOSPITAL

The organizational meeting of the staff of the new Physicians & Surgeons Hospital at Shreveport was held on December 12, 1947, after a dinner in the Physicians and Surgeons Cafeteria, with thirty-nine members in attendance. Dr. J. R.

Stamper was elected president, Dr. W. S. Harmon, vice-president, and Dr. Joe E. Holoubek, secretary. An executive committee consisting of Dr. L. W. Gorton, Dr. Wallace Brown and Dr. Keith Mason was appointed and will draw up the by-laws and constitution of the staff.

The Physicians & Surgeons Hospital is a new 106 bed hospital constructed under the guidance of Dr. J. R. Stamper near the Physicians & Surgeons Building. The architecture is modernistic in design, the building is completely air-conditioned and is so constructed that expansion will be easily made.

The staff of the Physicians & Surgeons Hospital is open to physicians who are members of the local and state medical societies.

GORDON MORGAN
1867-1948

Dr. Gordon Morgan, of Melville died on January 20. Dr. Morgan had been an active member of the State Society since 1915 and at the time of his death was Vice-President of the St. Landry Parish Medical Society.

WOMAN'S AUXILIARY, LOUISIANA STATE MEDICAL SOCIETY

The National Federation of Small Business, Inc., is sponsoring radio broadcasts on socialized medicine. So far there have been two discussions made by them over the radio on this subject. This is of particular interest to the Woman's Auxiliary to the Louisiana State Medical Society and material for distribution or information may be had by writing to: National Federation of Small Business, Inc., San Mateo, California. These pamphlets are splendid and were especially written to be read from coast to coast, so we urge you to get this material as we are sure you will find it of invaluable aid.

To emphasize the importance of these forceful talks, we quote the last paragraph of the second discussion:

> "Through these broadcasts and other activities we hope to arouse the professions to a realization of what is happening. We hope to make civic clubs and similar groups realize that it will take more than luncheon singing and meaningless speeches to give their clubs a purpose in life, and we want to reach labor leaders, big and little businessmen, workers in factories, farmers and all others in all walks of life, with the story, that ONLY in the greatest of unselfish and patriotic effort, can Americans live out their destiny of freedom and world leadership."

While we are on the subject of socialized medicine, if you will refer to your September, 1947 issue of the Reader's Digest you will find an article entitled "Our Most Dangerous Lobby". This article is written by Christian T. Herter, Member of Congress from Massachusetts. Also, "Our Most Dangerous Lobby—II", by Forest A. Harness, Member of Congress from Indiana, will be found in the December, 1947 issue of the Reader's Digest.

BOOK REVIEWS

A Text Book of Pathology: By E. T. Bell, M. D., 6th ed. Philadelphia, Lea & Febiger, 1947. Pp. 910. Illus. Pl. Price, $10.00.

This sixth edition of a work that has come to be accepted as a classical textbook has been thoroughly revised and is a worthy successor of the previous edition. It is a review of general pathology. The subjects discussed are necessarily brief but are comprehensive enough to be intelligible. The style is lucid and most readable. Although intended as a student text it can be read with much profit and enjoyment by the physician. The format is good. The paper and printing are most satisfying features. The index is thorough. The references are few but authoritative.

I. L. ROBBINS, M. D.

Philosophy and Medicine in Ancient Greece: By W. H. S. Jones, Litt. B., F. B. A. Baltimore, Johns Hopkins Press, 1946. Pp. 100. Price, $2.00.

This is a most interesting study and should prove of great interest and charm to the medical historian and philosopher.

I. L. ROBBINS, M. D.

Trichomonas Vaginalis and Trichomoniasis: By Ray E. Trussell, M. D.; with an introduction by E. D. Plass, M. D. Springfield, Illinois, Charles C. Thomas, 1947. Pp. 277. Illus. Pl. Price, $6.00.

This is the first comprehensive presentation of information concerning *Trichomonas vaginalis* and its relationship to vaginitis. The author is particularly well qualified to consider this subject because of his careful laboratory and experimental clinical studies on the subject.

The volume takes up in logical order the morphology of the three species of Trichomonas found in man, their methods of propagation and transfer from host to host, and the growth requirements of these flagellate organisms *in vivo* and *in vitro*. Dr. Trussell gives particular attention to the culti-

vation of *Trichomonas vaginalis* in a bacteria-free medium, which is his own achievement.

In Part II of the monograph attention is given to the organism and its relationship to diseases of the female and male genito-urinary organs. A clear point is made that bacteria-free *T. vaginalis*, when introduced into the vagina under aseptic conditions, will at times produce a vaginitis of moderate intensity and of a type which Dr. Trussell regards as relatively peculiar to this infection. On the other hand, experimental clinical infection may produce only a carrier condition. Part III considers treatment of *Trichomonas vaginalis*. The reviewer is impressed with the very large number of drugs which have been used in attempts to clear up the infection. Such an extensive array of chemotherapeutics and procedures indicates that none is preëminently a satisfactory therapeutic agent.

The book is well documented. Much of the material is presented in tabular form and there is an extensive bibliography as well as a satisfactory index. There are a few serious errors. One is the consistent misspelling of the word "pruritus". In the second place, when referring to the Trichomonas of the mouth, the author uses the specific names "*buccalis*" and "*tenax*" interchangeably, confusing the reader who does not realize that "*buccalis*" has in the recent literature been replaced by "*tenax*". Possibly the most serious criticism of the volume is the style, which tends to be verbose and repetitious. It is probable that the material could have been presented to better advantage in about one-half the space.

As is usual with Charles C. Thomas publications, the book is attractively printed and bound. Unfortunately, in the copy reviewed pages 13 through 30 are missing.

ERNEST CARROLL FAUST, M. D.

History of Medicine: By Cecilia C. Mettler, A. B., Ed. B., Ph. D. Edited by Fred A. Mettler, A. M., M. D., Ph. D. Philadelphia, Blakiston Co., 1947. Illus. Pl. Pp. 1215. Price, $8.50.

An historical work can only be measured accurately by the yardstick of time. However, Dr. Cecilia Mettler's "History of Medicine" promises to be one of usefulness particularly to the medical student whose desire for historical knowledge has been accelerated in recent years by newly formed societies, courses in medical schools, and by journals devoted to cultural and scientific history.

A grant provided by the Benjamin Salzer Fund enabled the author to devote nine years of patient labor to her task which was completed only a few days before her sudden death in 1944. The final editing and proof reading was done by her husband, the eminent Dr. Fred A. Mettler, Associated Professor of Anatomy, College of Physicians and Surgeons of Columbia University, who contributed the chapter on neurology and psychiatry. Early classical studies with formal training in history and in medicine had equipped Dr. Mettler for her work as historian. In 1939 she became Assistant Professor of Medical History at the University of Georgia Medical School, one of the first full-time teachers of medical history in this country. It was there that she initiated a graded series of lectures for each of the four years of the medical curriculum, and applied her correlated method of teaching to the plan of her published history.

According to the jacket, the book is intended for the practising physician and the lay reader as well as the medical student. Because of some surprising omissions of names, which the author confesses are "biographical gaps", the book will not completely satisfy those concerned with careful research and must be used with supplementary references, many of which are given in lists of selected readings that follow each chapter. Aside from minor flaws the general organization of the book is excellent and while the reading is necessarily sketchy at times and encyclopedic in form, the work is a fine achievement and will undoubtedly serve as a handy reference and guide for those who would seek more detailed information on some particular period or personality. Especially valuable are the volume's presentations of timely material and the fund of translations from ancient documents, for as the foreword tells us Dr. Mettler has "tracked down original sources, made her own translations, and compared these with previously constructed versions" . . . choosing the latter if her own offered nothing to be gained.

VERA MOREL

PUBLICATIONS RECEIVED

Appleton-Century Company, New York: Textbook of General Surgery (5th edition), by Warren H. Cole, M. D., F. A. C. S. and Robert Elman, M. D., F. A. C. S.

Grune & Stratton, New York: Psychopathology and Education of the Brain-injured Child, by Alfred A. Strauss and Laura E. Lehtinen.

W. B. Saunders, Philadelphia: A Manual of Clinical Therapeutics (2nd edition), by Windsor C. Cutting, M. D.; A Manual of Pharmacology (7th edition), by Torald Sollmann, M. D.; Minor Surgery (6th edition), by Frederick Christopher, B. S., M. D., F. A. C. S.; Sexual Behavior in the Human Male, by Alfred C. Kinsey, Wardell B. Pomeroy, and Clyde E. Martin.

Charles C. Thomas, Springfield, Illinois: The Pathology of Nutritional Disease, by Richard H. Follis, Jr., M. D.; Private Enterprise of Government in Medicine, by Louis Hopewell Bauer, A. B., M. D., F. A. C. P.

Williams & Wilkins Company, Baltimore: Blood Pressure and Its Disorders Including Angina Pectoris (2nd edition), by John Plesch, M. D., Budapest, M. D. Germany, L. R. C. P. and S. Edin. and Glas.